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NOTICES

MATERIAL FOR SUBMISSION:

Contributed papers on any phase of malaria or related subjects should be submitted to the editor. If suitable papers contain tables, require illustrations, or will require more than six pages in the Journal for publication, acceptance will be contingent upon the willingness of the contributor to assume the extra cost entailed by special typesetting; manufacture of cuts or over-run, which amounts are to be paid directly to the printer. Orders for reprints should be placed with the printers, and are to be attached to the galley proof when it is returned to the editor.

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MALARIA MORTALITY AND MORBIDITY IN THE UNITED STATES FOR THE YEAR 1942*

by

ERNEST CARROLL FAUST, *Department of Tropical Medicine, Tulane University of Louisiana, New Orleans, La.*

INTRODUCTION

It has once more been the privilege of the writer to make a yearly assay of malaria mortality and morbidity trends for the National Malaria Society, this time for the year 1942. Thanks are extended to the bureaus of vital statistics or other agencies of the departments of health of the forty-eight states and the District of Columbia for providing the basic information from which this report has been compiled. Acknowledgement is also made of the clerical assistance enthusiastically rendered by Mrs. Anne Richards and Miss Fay Gill, secretarial staff of the Department of Tropical Medicine of Tulane University.

PRESENTATION OF DATA

The basic summary data are presented in table 1. This provides information by states of the recorded malaria deaths and reported cases, together with the computed death rates and the ratio of deaths to cases. As indicated, only eight states (Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, South Carolina and Texas) had a 1942 mortality rate of 1.0 or more per 100,000 population, whereas there were ten states in this group in 1941, twelve in 1940 and 1939, and thirteen for each year of the decade 1929-1938. This information is set down for the fourteen southern states for the years 1935-1942 in table 2, and is graphically represented for the eight most malarious states in figure 1.

In 1941 there were twenty-nine counties (all in the South) with rates of 25 or more. These were distributed by states as follows: Arkansas, 4; Florida, 6; Georgia, 2; Louisiana, 1; Mississippi, 4; South Carolina, 7; Tennessee, 1; and Texas, 4. Only three of these had a rate of 25 or more for 1942 (Dixie County, Florida, rate: 42.8; Seminole County, Georgia, rate: 25.0; Williamsburg County, South Carolina, rate: 46.3). In addition, one county with a lower

*From the Committee on Statistics, National Malaria Society. Presented at the meeting of the Society with the Southern Medical Association, at Cincinnati, 1943.

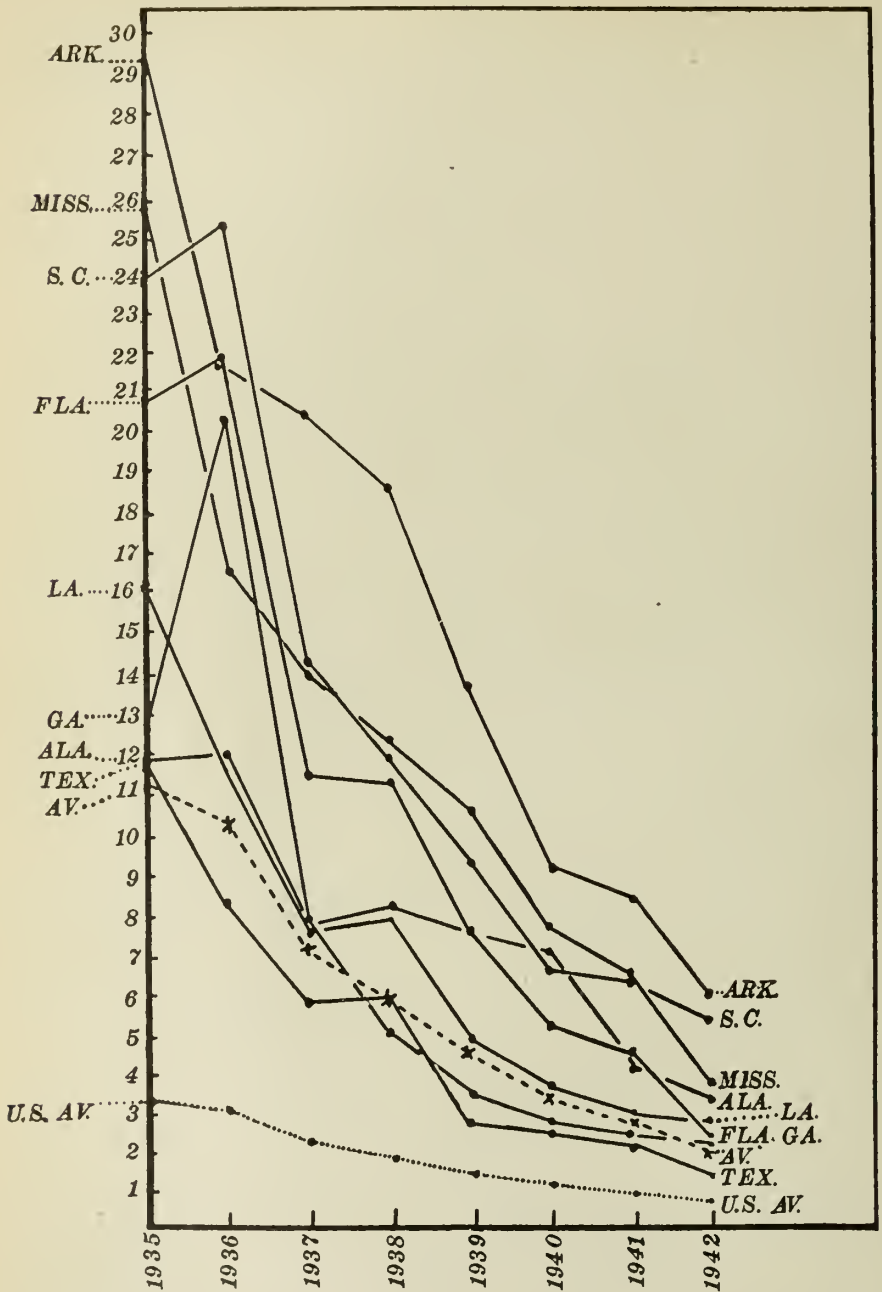


Figure 1—Graph showing the malaria mortality rate per 100,000 population for each of the eight most malarious states, the average rate for the fourteen southern states and the average rate for the entire United States for the years 1935-1942.

rate in 1941 reached the 25 level in 1942 (Bibb County, Alabama, rate: 25.0).

In spite of the very favorable condition that prevailed in 1942 with respect to malaria deaths, it has seemed advisable to scrutinize the county-by-county records to discover if there is any indirect evidence of an increase in 1942 over 1941. The evidence is scant but deserves being entered in the record. In Alabama, Bibb County alone showed an appreciable increase, with the highest rate since 1934. In Arkansas there were three counties, Ashley (highest since 1938), Craighead (highest since 1939), Phillips (highest since 1939). In Georgia there were two counties, Laurens (highest since 1938) and Washington (highest since 1938). In Kentucky Graves County had the highest number of malaria deaths since 1934. In Louisiana there were three parishes in this group, Caddo (highest since 1939), DeSoto (highest since 1936) and Natchitoches (highest since 1939). In South Carolina, Williamsburg County had the highest rate since 1934. In Texas, Bexar County had the highest rate since 1937. In Florida, Mississippi, Missouri, North Carolina, Oklahoma, Tennessee and Virginia there were no counties with 1942 rates appreciably in excess of 1941. Dixie County, Florida and Seminole County, Georgia, mentioned in the previous paragraph as having rates of 25.0 or more for 1942, actually had rates lower than in 1941. There is no evidence of resurgent malaria in any of the states on the Atlantic Seaboard north of South Carolina, in the Middle West, Southwest or on the Pacific Coast.

Malaria morbidity diagnosis and tabulation are still on a very unsatisfactory basis in so far as the records of the state departments of public health are concerned. There are states in the malarious areas in which deaths are reported without cases, while most of the state ratios between deaths and cases are so low as to be meaningless. It will be remembered that during epidemics or in hyperendemic areas the ratio may fall as low as 1:100 but that in mildly endemic territory it should be between 1:200 and 1:400. Only Mississippi approaches this latter figure (1:378). As in the last few years, states outside of malarious belts have indicated in their 1942 reports to the writer that the listed cases or deaths came from the Southern States. The total number of reported cases for the entire United States (58,963; see table 1) is probably about one-fourth to one-tenth of the actual number. This would suggest that 236,000 to 590,000 persons in the Continental United States had malaria in 1942 as compared with an estimated 278,000 to 695,000 for 1941 (Faust, 1943).

TABLE 1. *Malaria Data by States for the United States in 1942*

State	Total Deaths Reported	State Rate per 100,000 Population	Total Cases Reported	Ratio of Deaths to Reported Cases
Alabama	94	3.32	4369	46.48
Arizona	0	0	35	
Arkansas	118	6.05	1968	16.68
California	3	.04	83	27.67
Colorado	1	.09	3	3.00
Connecticut	0	0	2	
Delaware	0	0	0	
District of Columbia	0	0	5	
Florida	48	2.53	86	1.79
Georgia	76	2.43	981	12.91
Idaho	0	0	4	
Illinois	15	0.19	89	5.93
Indiana	8	0.23	6	0.75
Iowa	0	0	2	
Kansas	0	0	10	
Kentucky	12	0.42	36	3.00
Louisiana	60	2.56	420	7.00
Maine	1	0.12	0	
Maryland	1	0.05	13	13.00
Massachusetts	3	0.07	18	6.00
Michigan	3	0.06	24	8.00
Minnesota	0	0	1	
Mississippi	84	3.85	31,752	378.00
Missouri	20	0.53	95	4.75
Montana	0	0	1	
Nebraska	0	0	1	
New Hampshire	0	0	0	
Nevada	0	0	0	
New Jersey	3	0.07	20	6.67
New Mexico	0	0	14	
New York	1	0.08	8	8.00
North Carolina	33	0.92	248	7.51
North Dakota	0	0	0	
Ohio	4	0.06	8	2.00
Oklahoma	23	0.98	510	22.17
Oregon	1	0.10	50	50.00
Pennsylvania	4	0.04	10	2.50
Rhode Island	0	0	1	
South Carolina	100	5.26	10,017	100.17
South Dakota	0	0	0	
Tennessee	29	0.99	315	10.86
Texas	91	1.42	7,678	84.37
Utah	0	0	5	
Vermont	0	0	0	
Virginia	5	0.17	69	13.80
Washington	0	0	3	
West Virginia*	-	-	-	-
Wisconsin	0	0	0	
Wyoming	0	0	3	
Total for U. S.	841	0.65	58,963**	70.11

*No records received.

**Estimated to be one-fourth to one-tenth of the actual cases.

TABLE 2. *Malaria Mortality Rates of Southern States per 100,000 Population for the Years, 1935-1942*

State	1935	1936	1937	1938	1939	1940	1941	1942
Alabama	11.9	12.0	7.9	8.2	7.6	7.0	4.2	3.3
Arkansas	29.7	21.7	20.5	18.8	13.6	9.2	8.4	6.0
Florida	20.7	21.8	11.4	11.2	7.6	5.2	4.4	2.5
Georgia	12.6	20.2	7.6	5.0	3.5	2.8	2.4	2.4
Kentucky	3.0	1.8	1.0	1.2	0.8	0.63	0.6	0.42
Louisiana	16.2	11.4	7.9	8.1	4.9	3.7	3.0	2.6
Mississippi	25.9	16.4	14.0	12.4	10.5	7.6	6.7	3.8
Missouri	2.5	2.5	2.4	1.8	1.7	1.2	0.7	0.53
North Carolina	2.6	4.2	2.6	2.2	1.7	1.7	0.89	0.92
Oklahoma	4.4	3.7	3.7	3.3	2.5	1.0	2.2	0.98
South Carolina	23.8	25.2	14.2	12.1	9.1	6.7	6.6	5.3
Tennessee	7.7	5.3	3.6	3.6	3.3	2.1	1.7	0.99
Texas	11.9	8.2	5.9	5.9	2.8	2.5	2.3	1.42
Virginia	0.6	0.7	0.36	0.08	0.2	0.19	0.1	0.17
Average rate for 14 Southern States	11.2	10.2	7.0	5.8	4.5	3.4	2.73	2.02
Average rate for 48 States and D. C.	3.26	3.03	2.07	1.75	1.33	1.06	0.89*	0.65

*In the report for 1941 (Faust, 1943) this rate was erroneously published as 0.1055.

SUMMARY AND CONCLUSIONS

The malaria mortality data by states and counties for the United States in 1942 show a continued improvement over previous years. Only eight states had a rate of 1.0 or more per 100,000 and only four counties had a rate of 25.0 or more. The malaria morbidity data as reported by bureaus of vital statistics of the several states continue to be unreliable when tested against the expected ratios of deaths to cases. In mildly endemic territory, such as the malarious areas of the United States have become, it is estimated that there were between 236,000 and 590,000 cases in 1942 as compared with 278,000 to 695,000 in 1941.

REFERENCE

Faust, E. C. 1943. Malaria Mortality and Morbidity in the United States for the year 1941. *National Malaria Soc. Jour.* 2: 39-46.

RECENT RESEARCH IN PROPHYLAXIS AND TREATMENT OF MALARIA*

REPORT FOR 1942-1943

By HERBERT C. CLARK, M.D.
Panamá, R. de P.

The war has made it impossible to receive and review as much literature this year as is usually the case. This being an annual report to the National Malaria Society I have selected, chiefly, those relating to the present emergency. There are no doubt many important reports that have not been available and some that are restrictive or secret in character. For the busy civilian physician and field worker I am sure that the Tropical Diseases Bulletin, even during the war, can serve them well with their concise abstracts. I shall make this report as brief a collection of abstracts as possible from the material at hand.

White (1) in his review, states that the treatment of malaria is a subject of perennial interest and this in itself is an indication that finality has not yet been reached. The relative value of anti-malarial drugs in difficult circumstances and the manner in which they can best be employed are matters of outstanding importance at the present time. Java, which produced nine-tenths of the quinine in the world's markets, is in enemy hands. It is interesting to reflect how serious the situation might have been had Japan's aggressive designs been accomplished before Germany's pioneer research work had given us atabrin. He continues by directing our attention to the fact that there is not even uniformity of opinion regarding the manner in which quinine, the oldest and best tried remedy of all, should be administered and still less uniformity of opinion regarding the merits and demerits of the different remedies in the treatment of the acute attack of malaria and in clinical prophylaxis. He attributes some of this unsettled state of mind to the different degrees of malarial endemicity, difference in strains of the malaria parasites and to the different races of mankind. None of the specifics are capable of procuring *therapia sterilisans magna*.

Editorial (2): For a number of years the average consumption of quinine in India has been about 200,000 pounds annually. This is far below real requirements which can be placed, on a conservative estimate, at a million pounds. India supplies 70,000 pounds and imports 130,000 pounds. The present emergency forces the

*Partial Report of the Committee on Medical Research, National Malaria Society. Presented at the 1943 Meeting of the Society in conjunction with the Southern Medical Association, at Cincinnati.

serious consideration of the League of Nations advice regarding the short course of treatment and permit the patient's immunity full play.

Christopher (3) covered the field of cinchona derivatives and the synthetic drugs. He opposed the intramuscular injection of quinine, the intramuscular injection of atebtrin was not so harmful. He feels that in atebtrin (mepacrine) we have the only substitute for quinine.

Yorke (4) advocates the conservation of quinine stocks by its economic and efficient use in the treatment of malaria. He believes that nothing is gained by giving more than 20-30 grains of quinine a day in the acute stage. The treatment in use in Liverpool consists of the administration of 30 grains of quinine in solution by mouth, daily for 4 consecutive days and thereafter 20 grains every Saturday and Sunday for 8 weeks, or longer should a relapse occur. If the shortage of quinine stock should become severe the drug should be saved for those acute cases occurring in the unacclimated population.

Yorke (5) prefers quinine therapy but states that atebtrin (mepacrine) may be substituted in doses of 0.1 gm. thrice daily for seven days, followed by 0.2 gm. on Saturdays and Sundays for 8 weeks, and preceded, in severe cases, by injections of quinine. During the war it is important to conserve quinine. Mepacrine (atebtrin) should be used whenever possible.

Nicol and Shute (6) stress economy in the use of quinine. The amount of quinine necessary for cure varies according to the species of malaria. For *P. vivax* a single dose of five grains will abort an attack, and five grains once daily for 15 days will effect a cure of the febrile attack. Larger doses or extended treatment will not prevent relapses and this applies to patients bitten once by a single infected mosquito or by 100 infected mosquitoes daily for a week. In relapses even smaller quantities will suffice for a cure.

This experience was gained by the use of more than six strains of *P. vivax*. *P. falciparum* infections require 10 grains daily for 10 days, and this dosage is adequate for mixed infections. The so-called anti-relapse treatment is useless. Quinine should not be given after the cure of the first infection until relapse occurs, and then only when the diagnosis has been confirmed by blood examination. These men have had long experience with induced as well as naturally acquired malaria.

Covell (7) calls attention to the necessity of effecting an immediate reduction in the consumption of antimalarial drugs either by modifying our schemes of treatment or by increasing our efforts to reduce the incidence of the disease. It has come to be recognized that massive doses of anti-malarial drugs or the use of them over

long periods of time is not necessary. Relapse is independent of the dosage or duration of treatment. Short courses of treatment, frequently of only a week or even less in length, have therefore become the rule. The use of anti-malarial drugs over long periods when the infection is latent is not merely useless, but may retard the development of the defensive mechanism of the patient, without which the parasite cannot be eradicated from the body. The Fourth General Report of the Malaria Commission of the League of Nations (1937) presents the details regarding modern treatment. There are difficulties in framing a standard scheme of treatment appropriate for all circumstances. Different species of malaria parasites vary in their reaction to treatment and tendency to relapse and different local strains of each parasite show wide variations in this respect. There is a racial difference and people from non-malarial areas differ from those who have lived all of their lives in areas of high endemicity. The treatment offered by the League of Nations Commission was framed with considerable elasticity. The routine is quinine 15 to 20 grains, or atebirin 0.3 gramme, for 5 to 7 days followed in each case by 0.02 gramme plasmoquine daily for 5 days. No drug known, at present, destroys the sporozoits injected by the mosquito, and therefore no drug prevents malarial infection. Quinine or atebirin cut short a clinical attack and destroy the trophozoite stage of the parasite in most instances. No intensification of dosage or length of treatment will effect the radical cure of more than a certain percentage of infections. Plasmochin has no effect on the clinical attack but may reduce the percentage of relapses and may reduce the chances of mosquito infection. The physician's object is rather to tide the patient over the attack. The basic objects of treatment should be the prevention of death and the maintenance of malarious populations in a condition which will enable them to carry on their daily work. As a general guide, it is suggested that routine treatment should be limited to 15 grains quinine or 0.3 gramme atebirin, daily for not more than 5 days provided that clinical symptoms have by that time subsided. This may be followed by 0.02 gramme plasmochin daily for 5 days if available. Since supplies of anti-malarial drugs are at the present time strictly limited, rigid economy in the consumption of such drugs is essential.

Bryant (8) reports his experience with atebirin in the Sudan where *P. falciparum* infections were common and severe. He found that atebirin in doses of 0.3 gm. a day did not control severe malaria and that the drug combined with plasmoquine produced nausea and colic or vomiting. The combined use of atebirin and quinine made his patients feel exceedingly ill. He now uses atebirin in much larger doses than those usually recommended. He found that 0.6

or even 0.9 gm. a day produces no ill effects if plenty of hot, very sweet tea or sugar in some other form is taken. He feels that the parasitocidal action of atebtrin is not marked until the renal threshold of the drug has been reached; when the urine becomes bright yellow the temperature falls and improvement in the patient's condition is immediate.

Treatment of a severe case: Atebrin musonate 0.3 gm. is given intramuscularly and 0.3 gm. atebtrin by mouth on the first day. If the drug is vomited the injection is repeated after 3 hours. In serious cases a third dose of 0.3 gm. may be given, 0.9 gm. in all on the first day. On the second day 0.6 gm. is given in two doses and if nausea permits an injection of atebtrin musonate replaces the first dose. Thus, during the first two days from 1.2 to 1.5 gm. of atebtrin are given. Thereafter three tablets (each of 0.1 gm.) a day, in one dose after breakfast, are taken until 24 tablets in all have been given. Many people cannot tolerate more than 20 tablets. This course of atebtrin is followed after an interval of four days by quinine, 15 grains a day for four days. After another four-day interval two tablets of plasmoquine simplex (each of 0.01 gm.) three times a day for three or four days, if tolerated, complete the specific treatment.

A constant bitter taste in the mouth and some depression were the only toxic symptoms produced by these large doses of atebtrin. Nausea indicates the necessity for terminating treatment or reducing the dose of atebtrin towards the end of the course. Plenty of sugar prevents toxic symptoms. Splenomegaly and relapse are uncommon after this treatment.

Self-treatment by laymen in remote stations is encouraged and for this purpose a sheet of instructions is issued.

Meythaler (9) gives his experience on a large scale under war conditions and presumably of restricted quinine supplies. All cases given his method of treatment had to meet the following conditions:

- (1) The treatment must be started within two days of the onset.
- (2) The infection must be known to be due to a strain of low virulence.
- (3) The parasites must be relatively few in number.
- (4) The patient must be kept under close observation because of the possibility of a poor response or the development of a more severe type than at first believed.

Atebrin (mepacrine) was given three times a day for seven days in doses of 0.1 gramme each; two days' rest from drugs is allowed and then plasmoquine (pamaquin) is given thrice daily after food, for 3 days, in doses of 0.01 gramme each. For the more se-

vere cases the dose of atebtrin was doubled till the temperature became normal. In some, atebtrin musonate was given by the intramuscular route in daily doses of 0.3 gramme dissolved in 10 cc. distilled water till the temperature fell to normal. A very severe case on arrival was given 0.3 gramme atebtrin musonate by the intramuscular route at once; repeat the dose in ten hours and then continue the injections in fractional doses to the equivalent of 0.3 gramme twice daily until the temperature remains normal.

In 1,500 intravenous injections no serious trouble was experienced and some German clinicians prefer to give intravenous injections for the first few days in all cases of subtertian infection. Meythaler prefers the intramuscular route. The author claims that the relapse rate in benign tertian infections did not exceed 20 per cent. He attributed many of these to insufficient treatment. The author regards atebtrin as a perfectly safe drug with practically no contraindications.

Dove (10) is of the opinion that treatment should be determined solely by the symptomatic indications presented and not by the form of malaria. The minimum treatment prescribed for a case of malaria lasts about four weeks and consists of:

1. Atebrin, grains $1\frac{1}{2}$, three times a day, during the febrile period and 4 days thereafter.
2. Quinine, grains 5, four times a day for 7 days.
3. Atebrin, grains $1\frac{1}{2}$, three times daily for 5 days.
4. Quinine, grains 5, three times daily for 5 days.
5. Quinine, grains 5, and plasmoquine grains one-sixth, three times daily for 5 days.

In chronic, frequently relapsing cases the periods 3, 4 and 5 of the treatment are repeated after a ten days' interval. The author never saw a case intolerant of atebtrin though quinine idiosyncrasy did occur in some cases. He does not approve of intramuscular or intravenous methods of treatment.

Norman White (Trop. Dis. Bull. Vol. 39, No. 12, page 806) in discussing atebtrin feels that we have ample justification for the use of atebtrin daily, in a dose not exceeding 0.1 gm., to all susceptible troops exposed to the stress and strain of war in countries where subtertian malaria is prevalent. This method seems desirable over quinine for military needs.

Hill (11) recalls the difficulty in the last war due to subtertian malaria and expressed the opinion that with the aid of the synthetic drugs and quinine it should be possible to improve on the results obtained. He considers under-treatment as the greatest fault. He recommends for the treatment of the acute attack 0.1 gm. of atebtrin and 10 grains of quinine three times a day for 7 days. No toxic

signs or symptoms have been noted in 200 cases so treated. In severe cases these doses can be increased with advantage. During the next two days 10 grains of quinine hydrochloride are given three times a day. During the following 5 days 0.01 gm. of plasmoquine and 10 grains of quinine hydrochloride are given three times a day. The plasmoquine part of the treatment might be considered optional, perhaps, for cases treated in the field, but should be compulsory in the hospital. Intravenous treatment is essential at times if lives are to be saved. For anti-relapse treatment for those undergoing excessive strain, it is preferable to give one tablet, 0.1 gm. of atebtrin every day. Prolonged trial shows its harmlessness. Yellowing of the skin is of no consequence with troops at war. Statements regarding the toxicity of atebtrin have been much exaggerated. Manson-Bahr in discussing Hill's report states that he does not consider the intravenous or intramuscular administration of atebtrin as effective as quinine administered in like manner. He also feels that intramuscular injections of quinine can be of very great value. He agreed with Hill that relapses do not occur in persons with atebtrin-tinted skins.

Hughes (12) believes that the vast majority of clinical attacks of malaria in adult natives of hyperendemic areas requires no quinine or other specific treatment. The disease runs a mild course and terminates naturally. Europeans in such hyperendemic areas are exposed to very great danger and prophylactic measures with quinine or atebtrin should be used. In the treatment of attacks of malaria 30 grains a day are given during the acute stage, and a maintenance dose of about 5 grains a day. Injections of quinine are frequently required and intramuscular injections have advantages. There is no empirical finding to show that intravenous injections are superior to intramuscular injections. In comatose cases the intramuscular injection of quinine together with the intravenous injection of saline and glucose is remarkably successful. In all fever cases treatment should be given promptly. When the European leaves the hyperendemic zone treatment is advisable. For this the author recommends a course of atebtrin and quinine to be started 10 days after departure: 2 tablets (each of 0.1 gm.) of atebtrin and 2 five grain tablets of quinine daily for 7 days.

Smith (13) relates an experience with malaria on a Cruiser at war. During April and May of 1941 the personnel of a Cruiser, consisting of some 620 officers and men, were subjected nightly to the attacks of anopheline mosquitoes at the height of a malaria season. Experience taught him that it is dangerous to withhold specific treatment until the diagnosis has been confirmed by the microscope. No prophylactic use of quinine or atebtrin had been in

use. They developed 159 cases of acute malaria with two fatal cases. No doubt the difficulties were extreme in the management of such an epidemic on board a Cruiser engaged in active war service.

Weed (14) in his discussion of antimalarial drugs refers to the U. S. P. Totaquine now in use: a mixture of alkaloids from the bark of *Cinchona succirubra* Pavon and other suitable species of *Cinchona*. It contains not less than 7 per cent and not more than 12 per cent of anhydrous quinine, and a total of not less than 70 per cent and not more than 80 per cent of the anhydrous crystallizable *Cinchona* alkaloids, the designation *crystallizable alkaloids* referring to cinchonidine, cinchonine, quinidine and quinine. It is recommended the dose be 10 grains three times a day for seven days. He refers also to the therapy routines recommended by the Subcommittee on Tropical Diseases of the National Research Council:

1. Combined Q. A. P. treatment (method of choice):
 - (a) Totaquine or quinine sulphate, 10 grains thrice daily after food for 2 or 3 days or until the fever is controlled.
 - (b) Atebrin 0.1 gm. thrice daily after meals for the next five days.
 - (c) Two days without treatment.
 - (d) Plasmoquine 0.01 gm. thrice daily after meals for five days.

2. Atabrine-Plasmoquine Treatment:

Atabrine 0.1 gm. thrice a day after meals for 7 days, then two days' rest followed by 5 days of plasmoquine 0.01 gm. thrice daily after meals.

3. Totaquine or Quinine-Plasmoquine Treatment:

If no atebrin is available give totaquine or quinine as indicated in above for 7 days and during the last two days associate each dose of totaquine or quinine with plasmoquine 0.01 gm. thrice daily.

4. Suppressive Treatment:

Atebrin 0.1 gm. twice daily after food twice a week. Allow two or three days' interval between days of medication. It is recommended that pending more experience atebrin should only be given under the guidance of a physician or public health officer.

Kikuth (15) summarizes the use of atebrin and plasmoquine. Atebrin acts on the asexual forms of all the malaria parasites, but as a casual prophylactic it is just as inactive as quinine. Plasmoquine proved to be an anti-malarial substance of quite a new kind, in that it destroyed the crescents in malignant tertian malaria. It also exhibited another property, in that it lessened the relapse rate

in simple tertian malaria. . . . Unfortunately, however, large doses of plasmoquine are not entirely harmless. Notwithstanding its prophylactic action, casual prophylaxis is still impossible.

Hasselmann (16) described three cases of malaria in the Philippines who were given 0.6 gm. of atebirin during two days and then 0.03 gm. plasmoquine daily for 5 days, most of the doses being given intramuscularly, and who later relapsed with subtertian malaria, although they had remained in a malaria-free district. These cases illustrate the fact that plasmoquine may fail to prevent relapse. In Hasselmann's opinion quinine cannot be replaced by synthetic antimalarial compounds in the tropics. Peter (F. M.) criticizes the treatment as used by Hasselmann and disagrees with his conclusions. (*Trop. Dis. Bull.* Vol. 40, No. 1, p. 13).

Gamefar (17) is apparently the Italian synthetic product corresponding to plasmoquine and Italchina the Italian substitute for atebirin. The results of experience with these drugs are comparable with those usually expected with plasmoquine and atebirin.

Videla (18) refers to the Ascoli treatment of the chronic malarial spleen and suggests the following method which he has found successful. After quinine treatment, or in the period of full apyrexia, intravenous injections of 10 per cent solution of calcium chloride, in doses of 10 cc., are given daily or on alternate days to a total of 5 injections. Contraction of the spleen is observed within one-half hour of the injection and increases up to 1 hour, but the contraction passes off partially, leaving, at the end of two hours, the spleen permanently reduced to an appreciable extent and splenic pain disappears. These reductions are held to be due to augmentation of splenic tone due to the vaso-constriction induced by the drug.

Schoenback and Spingara (19) report two cases of malaria in drug addicts (heroin) in which the malaria was acquired by the intravenous injection of the drug by means of primitive apparatus shared by a number of addicts without any attempt at disinfection of any kind before or after use. In these cases an eye-dropper with a rubber nipple and a hypodermic needle were used.

A decade before the war the Malaria Commission of the League of Nations recommended the short courses of treatment for those who live in endemic regions. Such considerations were applicable for the most part only to civilians engaged in peace-time pursuits. In this war other considerations predominate. The Army is made up chiefly of young susceptible individuals exposed to the stress and strain of a tropical climate.

It is interesting to note seven of the abstracts in this report all consider atabrine as a safe drug under ordinary dosage yet most all

of them report the toxicity of plasmoquin if given for more than three days in ordinary dosage.

Our personal experience with plasmoquine in doses of 0.01 gram three times a day for 5 days is that one out of 10 will suffer from the toxic effects of the drug. We do not use the drug in the field any more because of this difficulty and also because we do not see that we have gained any benefit from its use as a gametocide nor as assistance in preventing relapses in the field. This may not conform to hospital experience where the drug can be under the control of a good staff of doctors and nurses.

The Chagres River villages (20) of our Santa Rosa Malaria Station have been on bimonthly thick blood film surveys followed by treatment of all found positive for parasites. An inspection trip was made each month between surveys and blood films taken from any who claimed to be sick. These were treated for malaria if parasites were found.

Half of the group in the villages was treated with atabrine (American product) 0.1 gm. three times a day for five days. The other half was treated with quinine sulphate tablets, 18 grains a day for five days. Since we use 3 grain tablets for children, it was easier to double the dose for adults, therefore 18 grains rather than 15 grains a day were given. The atabrine tablets were always broken, at least into two pieces, before administration to insure disintegration. No plasmoquin was used in either group.

The control village situated on a similar arm of Gatun Lake was permitted to use either atabrine or quinine if they cared to use treatment voluntarily but they had to call on some official to see whether they were on the positive list for malaria following each survey. Some of them really treated themselves.

The average bimonthly parasite rates were as follows: Quinine group, 8.9 per cent; atabrine group, 10.9 per cent; control group, 25.6 per cent. The cumulative rates for the year's surveys were respectively 20.9, 30.5 and 45.7 per cent. The relapse rate was lower than usual this year and there was no death due to malaria in any group. No babies from birth to twelve months of age were found positive in the treated groups but 5 out of 14 such babies in the control group were found positive for malaria. It should be stated that the entire isthmian area, whether in controlled regions or not, has shown an unusual decline in malaria since March, 1943 to date (September 1943). Even the hospitals of the area failed to note any increase in malaria in June and July as is usually the case during those months. The concensus of opinion based on the scientific visitors to our region and on the literature received indicates quinine is still the drug of choice if available, atabrine next and totaquine

(U. S. P.) for the less important services. Opinion is divided about the use of plasmoquin but all admit the danger attending its use in the field and nearly all agree that atabrine, in ordinary dosage for treatment or prophylaxis, is harmless.

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RECENT RESEARCH IN AVIAN AND SIMIAN MALARIA*

REDGINAL I. HEWITT**

It has been the policy for a number of years of the Committee on Medical Research of the National Malaria Society to prepare reviews of contemporary research in various fields of malariology. Since the entrance of the United States into the war, interest in malaria has increased tremendously in this country, and many laboratories in universities and industrial organizations are engaged in various phases of research on malaria, using birds and monkeys as experimental hosts. Much of this work is under government contract, and progress and results cannot be revealed at the present time. Similarly, little of the work on malaria which is being carried out in European laboratories is being published. The present report, therefore, includes only material which has been published in recent American and foreign journals. The work is dated from the reports presented to the National Malaria Society for the 1941 meetings by Doctors Martin D. Young and J. C. Swartzwelder on avian and simian malaria respectively. Abstracts in the Tropical Diseases Bulletin have been used freely when the original journals were not available to the reviewer, and papers up to October 1, 1943, are included.

AVIAN MALARIA

Host records and new species. A new species of avian *Plasmodium* in fowls (*Plasmodium juxtannucleare*) has been described recently by Versiani and Furtado Gomes (1941) from the state of Minas Gerais, Brazil. This parasite apparently resembles *P. vaughani*, *P. rouxi*, and *P. nucleophilum* because of its small size, but is more like *P. nucleophilum* because many of the forms are in direct contact with the nucleus. The number of merozoites per segmenter is 3 or 4, rarely 5, and most of the gametocytes are oval or round. *Gallus gallus domesticus* is the type host, and of eleven other species of birds experimentally inoculated, including sparrows, canaries, turkeys and pigeons, only one of two turkeys was susceptible. In a later paper (1943), the same authors give further notes on experimental infections. They describe rather heavy infections in young chickens, one reaching 5,984 parasitized red cells per 10,000 at the

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peak of parasitemia. A mortality of 75 per cent within two weeks after infection in young chickens is reported. Older birds are apparently more resistant. Beltrán (1941) has also reported the occurrence of *P. juxtannucleare* in a chicken from the state of Chiapas in Mexico. This parasite and *P. gallinaceum* are the only plasmodia which have yet been found to occur naturally in the domestic fowl, and *P. juxtannucleare* is the only malaria parasite yet found in chickens from the Western Hemisphere.

Shortt, Menon and Seetharama Iyer (1941) have made the observation that wherever *P. gallinaceum* has been discovered in domestic fowls in India the wild jungle fowl is present in adjacent forests. In 1 of 40 wild fowls examined, *P. gallinaceum* was found and was transferred successfully to domestic fowls. They conclude, therefore, that the wild jungle fowl is the natural host of *P. gallinaceum*.

An avian malaria parasite in turkeys from different localities in Kenya is described by Purchase (1942). This parasite has been named *P. durae* by Herman (1941). It is highly fatal to young poults and transient infections can be produced in chicks. Purchase remarks that ducks and adult chickens are refractory.

In the United States, Wetmore (1941) describes the results of a survey of blood parasites from birds of the District of Columbia, Jordan (1943) and Thompson (1943) from birds of Georgia, and Wood and Herman (1943) from birds in the Southwestern United States.

Host-parasite relations. Wolfson (1941) evaluates the use of various avian hosts for malaria research and concludes that the duck is the most suitable for several reasons, among which are mentioned their susceptibility to several species of *Plasmodium*, large size, low cost and adequate supply. The duck as a host for avian plasmodia is further discussed by Manwell and Hathaway (1943), and Manwell (1943). Hewitt (1942), and Hewitt, Richardson and Seager (1942) give the results of their studies on a large number of untreated infections with *Plasmodium lophurae* in white pekin ducks, and present data on the normal blood picture and temperatures of unparasitized and parasitized ducks. It is apparent that the duck as a host for experimental work in malaria is fast replacing the canary in this country for many types of research. *Plasmodium lophurae* in the duck is being used in many laboratories throughout the United States, and the "3T" strain of *Plasmodium cathemerium* (Wolfson, 1943) also produces infections in ducks which are useful for certain studies, particularly chemotherapy. It is comparatively simple to produce uniform infections with both of these host-parasite relationships throughout an unlimited number of subinocula-

tions, and the comparisons thus afforded between results obtained in different laboratories using essentially the same techniques are exceedingly helpful.

Manwell and Nadler (1942) find the asexual cycle of *P. vaughani* in the canary to be 24 hours in length, with low synchronicity. A tendency for the parasites to invade immature red cells was noted. Variations in the asexual cycle of *Plasmodium relictum* from the pigeon when transferred to canaries are described by Redmond and Prather (1943).

Beltran and Vargas (1942) find that the prepatent period of *P. gallinaceum* in chickens following intravenous inoculation with sporozoites is 7 to 11 days.

Mosquito transmission. Because of the increasing interest in the use of *P. lophurae* in ducks and chickens for experimental purposes, several attempts have been made to obtain a good vector for this parasite. Laird (1941) has tried *Culex restuans*, *Aedes atropalpus*, *A. albopictus*, *A. aegypti*, and *Culex pipiens*, and found the first three species to be susceptible. Transmission with *A. albopictus* was demonstrated, but with difficulty. Laird comments that the presence of apparently mature sporozoites in the salivary glands of mosquitoes does not always indicate ability to infect a susceptible animal.

By selected breeding from infected females of a strain of *A. aegypti*, Trager (1942) developed a strain which after a year of mass non-selective breeding has maintained its character of being more susceptible to infection with *P. lophurae* than the stock from which it was derived. Hurlbut and Hewitt (1942) succeeded in transmitting *P. lophurae* in ducks with *Anopheles quadrimaculatus*, but in only a few birds, and the infections produced were low grade.

Thus far, it has not been possible to produce severe infections with *P. lophurae* by mosquito transmission in either chicks or ducks. *Aedes albopictus* appears to be the best vector yet found, and it is far from satisfactory.

Vargas and Beltran (1941) report one specimen of *Culex quinquefasciatus* accidentally infected with *P. gallinaceum*, and state that abundant sporozoites were found in the glands. *Armigeres* and *Aedes* species were found to be good transmitters of *P. gallinaceum* by Russell and Menon (1942) but it was not possible to infect anophelines even when fed simultaneously with *Armigeres* and *Aedes* mosquitoes which become 100 per cent infected. Oocysts were found in one specimen of *Culex mimuloides* fed on a fowl infected with *P. gallinaceum*. Various mosquito hosts of *P. gallinaceum* found in India are discussed by Russell and Mohan (1942).

Beckman (1942) gives infection rates with the 3H2 strain of

P. cathemerium in canaries transmitted by the bite of 1 infected *Culex pipiens*. Of 60 experimental birds, 46 became infected and 44 died, a mortality of 95.6%.

Exoerythrocytic bodies and the development of sporozoites in the vertebrate host. Studies on the exoerythrocytic forms found in infections with certain species of avian plasmodia continue to occupy the attention of a number of investigators. Adler and Tchernomoretz (1941) report continued passage of exoerythrocytic forms of *P. gallinaceum* in the apparent absence of erythrocytic schizogony. They eliminated the pigmented stages in red cells by administering 150 mgm. per kilogram doses of quinine hydrochloride, which did not affect the EE bodies. When brain emulsions from infected fowls which had been treated with quinine hydrochloride were inoculated into clean fowls, and the bird was then placed on quinine dosage, EE bodies developed but the pigmented forms were eliminated by the quinine. Five passages were made in this manner. A cessation of quinine treatment allowed the development of pigmented stages in the red blood cells.

Considerable difference of opinion still exists regarding the exoerythrocytic development of sporozoites following their introduction into avian hosts. Kikuth and Mudrow (1941) assert that all sporozoites in salivary glands are mature, and that the changes in nuclear structure which have been described by Missiroli on several occasions are the result of the drying technique used in preparing slides. They believe that development of the sporozoites within a freshly infected host occurs only after a delay period of several hours. The uninucleate sporozoite becomes a uninucleate rounded body which can be seen within 16 hours in the cells of the reticulo-endothelial system, either at the site of injection or in visceral tissues. Nuclear multiplication then occurs within 2 or 3 days, releasing merozoites which penetrate either red cells or other reticulo-endothelial cells. Missiroli (1942) argues that Kikuth and Mudrow mistake the ordinary developmental forms of avian malaria parasites for the immediate developmental forms derived from sporozoites. He reasserts his previous viewpoint that the early development of sporozoites takes place extracellularly in lymph spaces and not within histiocytes. The division and migration of chromatin masses, as first described by Missiroli, has also been seen by Schulemann (1942). Sporozoites of *P. cathemerium* were mixed with trypan violet and injected into the pectoralis major muscle of canaries. The site of injection was excised within 24 - 99 hours, at intervals, fixed and sectioned.

Zain (1941) states that in fowls infected with sporozoites of *P. gallinaceum* the first forms to develop are EE bodies. The mero-

zoites from these give rise to other EE bodies or to erythrocytic pigmented parasites. When blood containing erythrocytic forms only was inoculated intramuscularly the first forms to develop were within erythrocytes, and only after approximately 2 weeks did EE bodies appear in the brain. EE bodies in the brain of fowls infected with sporozoites of *P. gallinaceum* have been found as early as the 5th day by Seetharama Iyer, Shortt and Menon (1941). Corradetti (1942) states that *P. gallinaceum* and similar parasites are able to infect cells of the reticulo-endothelial system as well as red cells, but the former only as long as no immunity or balance between host and parasite exists.

Studying the tissue distribution of EE bodies in sporozoite induced infections with *P. cathemerium*, Porter (1942) found that the early stages occurred only in the liver, spleen and bone marrow. Later they were abundant in endothelium and capillaries, as well as in local intravascular accumulations of macrophages.

In spite of the large amount of work which has been done on the exoerythrocytic forms of certain species of avian plasmodia within the past few years, many gaps still exist in our knowledge of the nature and function of these forms. It seems quite well established that they are part of the life cycle of *P. gallinaceum*, and of certain strains of other species, whether the infections are produced by sporozoites or by asexual forms. It also seems quite clear that the sporozoites of these species of avian plasmodia undergo a certain period of development outside the red cell (whether in histiocytes, lymph spaces, or reticulo-endothelial cells) before becoming pigmented parasites within erythrocytes. It has still not been proven, however, that the fate of sporozoites of human or simian malaria undergo similar development, nor have exoerythrocytic stages been proven to exist at any time in the life cycle of human or simian malaria.

Chemotherapy. The recent loss of our source of supply of quinine has stimulated a broad coordinated program on the chemotherapy of malaria in the United States, particularly the search for new synthetics. As mentioned earlier, however, most of this work is being carried out under wartime restrictions and details cannot be released at the present time. The papers described below appeared either before restrictions on publications were invoked, or concern the mechanism of action of known antimalarials.

Beckman (1941) describes the retardation of schizogony by atabrine in *P. cathemerium* infections in canaries, stating that this effect is the most promising criterion of the action of this drug. Diminution of pigment, accentuation of vacuolization and a reduction in the number of merozoites were noted also. A similar inter-

pretation of the action of atabrine on *P. cathemerium* is given by Boyd and Dunn (1941).

Hegner *et al* (1941a, 1941b) demonstrate the plasmodicidal effect of hydroxyethylapocupreine dihydrochloride on *P. lophurae* infections in ducks, *P. relictum* in pigeons and *P. cathemerium* in canaries, stating that its advantage over quinine is in its lower toxicity. In addition, 21 sulfonamide derivatives were tested, using the tubing method of administration 3 times daily, and no marked effects were produced by any of them on blood induced *P. lophurae* infections in ducks. Using the drug diet method, Walker and Van Dyke (1941) found that sulfathiazole and sulfadiazine were effective against blood induced infections with *P. lophurae*. Sulfanilamide was much less effective. Marshall, Litchfield and White (1942) state that the maintenance of a more or less constant blood concentration of a sulfonamide drug for a sufficient length of time is just as important for effective therapy in *P. lophurae* infections in ducks as it is in bacterial chemotherapy. Using the drug-diet method they tested a large number of sulfonamides and found several of them to be effective. A definite antagonistic effect by paraaminobenzoic acid on the antimalarial action of sulfonamides was demonstrated.

The action of "Acranil," an atabrine derivative, on *P. cathemerium* in canaries is reported by Gingrich and Fillmore (1942). They state that "Acranil" compares favorably with atabrine, but the duration of its effect is somewhat shorter. No effect was produced on *Haemoproteus columbae*.

Fulton (1942) attempted to produce a plasmochin-resistant strain of *P. gallinaceum* in fowls (See Fulton and Yorke, 1941, for studies on the development of plasmochin-resistance in *P. knowlesi*) during 33 passages over 15½ months without success. He concluded that the resistance of EE bodies in this species might account for the failure to produce drug resistance.

The reproductive rate of *P. lophurae* in ducks is used as an indicator of the chemotherapeutic effects of quinine by Waletzky and Brown (1942, 1943). Reproduction was inhibited by 40-minute to 4-hour *in vivo* exposures to quinine, and no evidence was obtained of indirect action through a metabolite. Inhibition of reproduction was obtained by a much lower concentration of quinine *in vivo* than *in vitro*.

Seeler, Dusenberry and Malanga (1943) have studied comparatively the action of quinine, quinidine, cinchonine, cinchonidine and quinoidine against blood induced *P. lophurae* infections in ducks, and find that all show about the same degree of activity with the exception of quinoidine, which was considerably less ac-

tive. Two samples of totaquine were found to be as active as quinine.

A review of the literature on the chemotherapy of avian malaria is given by Marshall (1942). Experimental methods, therapeutic effects, the action of drugs on different stages of the parasites, species and strain variation, drug fastness, *in vitro* studies and mechanism of action are all described critically.

The direct plasmodicidal effect of quinine, atabrine and plasmochin on *P. lophurae* is described by Hewitt and Richardson (1943). Degenerative changes in the parasites following the administration of these drugs are described and illustrated, and experimental data is presented to show that degenerate parasites are incapable of producing the same type of infections upon subinoculation as those produced by parasitized blood from untreated donors.

The chief advances which have been made within the past two years in the experimental chemotherapy of avian malaria are (1) the development of standardized host parasite relationships for testing new drugs, (2) the use of the drug-diet method for administering drugs in certain cases where it has been shown that a constant blood concentration increases the therapeutic effect, (3) the stimulation of interest in the synthesis of totally new organic chemicals, unlike quinine, atabrine, or plasmochin, for experimental testing, (4) the appropriation of federal funds to many investigators for a concerted attack on the problem of antimalarials, and (5) the co-operation of organic chemists in industrial organizations and universities in supplying a large number of new compounds for testing.

Immunity. P. F. Russell and his coworkers, working in India, have recently published several interesting papers relative to the immunization of fowls against *P. gallinaceum* by the introduction of antigens prepared from killed, inactivated sporozoites or vaccines prepared from sporozoites or ground thoraces. Russell, Mulligan and Mohan (1941) inactivated sporozoites by exposing them to ultra violet light. These stimulated the production of agglutinins when injected into fowls but produced no infection. The serum from these fowls agglutinated sporozoites freshly dissected from salivary glands. The inactivated sporozoites were then used as a vaccine (Mulligan, Russell and Mohan, 1941), and although infections occurred in the vaccinated animals, the pathogenic effect varied with the agglutination titre of the serum. When fowls were immunized by repeated injections of both vaccine (in this case, dried thoraces of infected mosquitoes) and serum, a high degree of immunity was obtained (Russell and Mohan, 1942). The serum of chickens immunized with the antigen prepared from ground thoraces of infected mosquitoes gave a high agglutination titre, and such chickens

developed only a mild infection when bitten by infected mosquitoes. No such protection was given against trophozoite-induced infections (Russell, Mulligan and Mohan, 1942). An increased spleen volume caused by chronic malaria, by serum treatment, by sporozoite vaccination and by chronic malaria following sporozoite vaccination with and without serum treatment is recorded by Russell, Mohan and Putman (1943).

Vezzoso (1941) injected into fowls infected with *P. gallinaceum* large doses (20-25 cc/Kilo) of serum from fowls which had recovered from infection within 10 to 50 days. Some immunity was claimed when the serum dosage was continued throughout the infection.

The acquired immunity to *P. lophurae* of chickens over 3 weeks old was interfered with by the simultaneous injection of carbon ink into the peritoneal cavity and the intracardial, intracerebral or intraperitoneal injection of parasites, according to a report by Trager (1941). This is claimed to be due to the blockage of the lymphoid macrophage system.

G. Boyd and Gilkerson (1942) state that when parasites (*P. cathemerium*) from previously uninfected canaries are introduced into latent birds, the merozoite number in mature segmenters is reduced. Moreover, gametocytes were removed from the blood of latent birds (upon reinoculation with fresh parasitized blood) less rapidly than the asexual forms.

General. In 1942 a Committee on the Terminology of Strains of Avian Malaria was appointed by the American Society of Parasitologists, its purpose being to allocate specific designations to various strains and species of avian plasmodia being carried in various laboratories throughout the United States. A report was prepared by this committee (Huff, G. Boyd and Manwell, 1942) in which designations consisting of combinations of numerals and letters were assigned to different strains. It was urged that before publishing results of work on new strains or substrains investigators secure designations from the committee for such strains and incorporate them in their publications. This suggestion has been complied with by a number of investigators and the continued use of single strain designations specified by the committee should prove helpful in eliminating confusion caused by the multiple names for strains used in the past.

Attempts to produce infections with malaria in birds by the oral route have been continued by a number of investigators. (See reviews of earlier papers on this subject by Young, 1943.) Beltran and Vargas (1941) obtained no infections when sporozoites of *P. gallinaceum* were introduced orally into chicks. Doses of from 1 to

8 pairs of infected glands were used. Paraense, Ferraz Franco and Menezes (1942) were unable to transmit *P. gallinaceum* by introducing infected red cells orally into chicks. Wolfson (1942), on the other hand, obtained an infection in 1 out of 4 canaries to which tissues of canaries containing erythrocytic and exoerythrocytic stages of *P. cathemerium* were administered by mouth.

Trager (1941, 1943) describes in considerable detail his methods for keeping *P. lophurae* in a viable condition *in vitro*. In the first paper he states that survival *in vitro* at temperature of 39.5° to 42° C. is favored by a balanced salt solution having a high potassium content, by aeration but not high oxygen tension, by an optimal density of parasites, by frequent renewal of the suspending medium, by concentrated red blood cell extract, optimal concentrations of plasma, serum, chick embryo extract, glucose or glycogen, glutathione, yeast extract and liver extract. Some evidence was obtained of multiplication of the parasites on the first day, and more than 30 per cent of the parasites were viable on the third day. In the second paper survival of *P. lophurae* for about two weeks *in vitro* at 40°-41° C. was achieved. The medium consisted of duck red cell extract in balanced salt solution, with glutathione and glucose or glycogen, serum, embryo extract and calcium pantothenate (0.02 mg. per ml.). One-half of the medium was replaced daily with fresh medium and fresh red cells were added every 2 days. Gentle agitation was applied throughout. Although Trager's results do not yet demonstrate successful concentration of malaria parasites, they are certainly encouraging, and further trials of media of the sort described may lead to a practical method for cultivating plasmodia *in vitro* for short periods of time at least.

Pursuing another line of investigation, Trager (1942, 1943) reports on the influence of biotin upon susceptibility to malaria. Young ducks and chickens were rendered biotin-deficient by feeding them diets containing 25 per cent dried egg white. Birds on this biotin-deficient diet developed much more severe infections with *P. lophurae* than did non-deficient control animals. Similar results were obtained with *P. cathemerium* in ducks. The injection of biotin into animals fed a diet adequate in this vitamin had no plasmodicidal effects, and Trager believes this may be due to the fact that excess biotin was removed rapidly from the blood. If similar results can be demonstrated in human malaria, new light may be shed on some of variations in the severity of infection which occur with various species of human plasmodia, not only with regard to biotin, but possibly in the case of other vitamin deficiencies as well.

Brooke (1942) attempted to inoculate canaries with *P. cathemerium* and *P. relictum* by introducing sporozoites freshly isolated

from supposedly mature oocysts. Seven single oocysts were isolated and injected with negative results, indicating that sporozoites are probably not infective until they have left the oocysts.

A fatal case of apparently naturally acquired malaria in a canary is recorded by Herman (1942). This bird was obtained from a fancier in a suburb of Los Angeles, and had been kept in an outdoor flying cage. At autopsy, one-third of the cells in the heart blood were infected with *P. cathemerium*. It has been assumed too frequently that canaries used for experimental purposes in avian malaria research are parasite-free when obtained from breeders. This case should certainly demonstrate the advisability of inquiring very carefully about the source of canaries used for experimental purposes, before their purchase.

Methods for the preservation of avian malaria parasites by low temperature freezing are described by Manwell *et al* (1942, 1943), and parasites were kept in a viable condition for as long as 244 days.

Lack (1942) describes intravascular agglutination in canaries infected with *Plasmodium cathemerium*. Large agglutinated masses of red cells, permanent thromboses and extensive tissue damage in living birds were seen with the aid of a quartz rod illuminator. Death of the birds followed these changes. According to Hill (1942) anemia is the cause of death in pigeons infected with *P. relictum*.

According to Devine and Fulton (1942) the pigment formed by *Plasmodium gallinaceum* is haematin.

Velick (1942) studied the respiratory metabolism of *P. cathemerium* during its developmental cycle in the Warburg apparatus. Oxygen consumption increased slowly during growth of the parasites, but was accelerated greatly when nuclear division commenced.

Attempts to infect man with *P. relictum* are reported by McLendon (1943). It was found that this parasite remained viable in the human circulatory system for as long as 4½ hours, but not for 8 hours.

A review of recent work on *P. gallinaceum* is given by Beltran (1942), and Young (1942) has reviewed the work on avian malaria up to the middle of 1941.

SIMIAN MALARIA

Very little work has been published on simian malaria during the past two years, probably because of the difficulty in obtaining monkeys for experimental purposes from India and South America. Recently, however, several shipments of *Macacus rhesus* monkeys

have reached this country and it is believed that the shortage of this experimental host will be relieved gradually.

The nature of the pigment of *P. knowlesi* has been investigated by Devine and Fulton (1941) and by Morrison and Anderson (1942). These investigators submitted the pigment to chemical and spectroscopic examination and concluded that it was haematin. Anderson and Morrison (1942) inoculated solutions of disodium ferrihaemate into monkeys and compared the pathology with that produced by *P. knowlesi*. The pathology was qualitatively similar, differing only in degree. They express the opinion that the mechanism of injury in *P. knowlesi* infections in monkeys is anoxemia, due to vascular occlusion superimposed on severe anemia. In another paper the same authors (Morrison and Anderson, 1942) conclude that ferrihaemate is not the causative agent of malaria paroxysms, since the pigment is not liberated in soluble form.

The pathology of *P. knowlesi* in *Macacus rhesus* is described by Rigdon and Stratman-Thomas (1942). Tissues from twenty-six monkeys which were either killed or died during the acute phase of the disease were studied. Lesions described are similar to those reported in human malaria infections. The presence of dilatation of the cavities of the heart, edema of the lungs, dilatation of sinuoids around the central veins of the liver, necrosis of hepatic cells and parenchymatic degeneration of the kidneys suggested that anoxemia might be the important factor in the cause of death.

Fulton and Yorke (1941) produced a plasmochin-resistant strain of *P. knowlesi* by repeated treatment and transfer. In the first monkey infections could be controlled by 4 daily intramuscular injections of 3.3 mgms. per kilogram of plasmochin, with relapse occurring within 2 to 6 days. After transfer to another monkey 13.2 mgms. per kilogram of plasmochin failed to control the infection, and similarly after another transfer a high dosage of the drug did not affect the course of the infection.

Dikshit (1941) withdrew 80 per cent of the blood from an immune monkey and replaced it with non-immune blood, and found that immunity to superinfection was not lost. When more than 70 per cent of the blood of a normal monkey was withdrawn and replaced by immune blood, the animal acquired an immunity. Repeating the same experiment, using an infected monkey instead of a normal monkey, the monkey was cleared of most of its infection and passed into a chronic state.

Agglutination antibodies have been demonstrated in the blood of monkeys infected with *P. knowlesi* by Ray, Mukerjee and Roy (1941). These antibodies increased in titre with the increase in

duration of chronicity, and showed a rise in titre when superinfection was carried out.

In metabolism studies on *P. knowlesi* *in vitro*, Wendel and Kimball (1942) found that parasitized blood shows unusual ability to produce pyruvic acid. A correlation between the degree and stage of the infection and the rate and extent of pyruvate formation was noted. The carbohydrate metabolism of *P. knowlesi* is further described by Wendel (1943). It was found that parasitized blood consumes oxygen and destroys glucose *in vitro* with great rapidity as compared with blood from normal animals. Approximately one-half of the destroyed glucose was converted to lactic acid and the remainder was only partially oxidized. Anaerobiasis stimulated glycolysis by infected red cells, but had no effect on normal erythrocytes. It was concluded that low degrees of parasitemia, dilution of serum and neutralization of accumulated acid are favorable to prolonged active parasite metabolism.

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MALARIA PREVENTION ACTIVITIES OF STATE BOARDS OF HEALTH 1943*

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In an effort to obtain information of current malaria prevention activities of State Boards of Health of Southern States, a questionnaire was forwarded to the various states requesting certain information as to such activities conducted during the past year. Replies were received from thirteen states. These replies reflected, almost entirely, (1) the fact that former state programs had been seriously interrupted by the loss of trained personnel to war connected activities, and (2) that present activities of these states directed toward malaria prevention consisted almost entirely of the program of Malaria Control in War Areas carried on in cooperation with the U. S. Public Health Service. This change apparently resulted in stopping or seriously curtailing activities in many malarious areas, in which prevention activities were formerly conducted, and the inauguration of such activities in numerous new areas in the vicinity of Army, Navy or war industry establishments. The information obtained from the questionnaires and from other sources, however, indicates activities were conducted in a large number of areas in the various states and that intensive programs, involving both drainage and larvicidal work, were carried out.

All thirteen states reported utilizing drainage as a means of obtaining control of mosquitoes and in reducing the need of larvicidal work. Considerable major drainage work was accomplished, as four states, Arkansas, North Carolina, South Carolina and Texas, reported doing machine ditching, and seven states, Alabama, Arkansas, Florida, Kentucky, North Carolina, Oklahoma and South Carolina, reported utilizing dynamite, while all thirteen states reported using hand ditching for both major and minor drainage work, though the majority of the hand ditching was classed as minor drainage. Three states, Mississippi, South Carolina and Tennessee, reported installing varying amounts of permanent lining of ditches in which both precast and monolithic concrete linings were used. Two states, Mississippi and Tennessee, reported in-

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stalling underground drains in several areas. While all the states did not report the amount of water area eliminated, it is apparent from those which did that a considerable amount of water area was permanently eliminated by the drainage operations. All states reported a large amount of brushing, clearing and rechannelling of non-drainable water areas and existing ditches to facilitate larvicidal operations.

All states reported conducting extensive larvicidal operations in war areas. Several states mentioned the continuation of the activities of the Tennessee Valley Authority. Three states, Alabama, Georgia and Mississippi, made specific mention of county and city sponsored malaria prevention activities under State Board of Health direction, not connected with the Malaria Control in War Areas program; one state, Mississippi, mentioned the continuation of activities of the Corps of U. S. Engineers on flood control impoundments; and three states, Alabama, Georgia and Tennessee, mentioned continuance of work on major hydroelectric impoundments. One state, Texas, reported operations against both *A. quadrimaculatus* and *A. albimanus*, and three states, Florida, Louisiana and Texas, reported carrying on *Aedes aegypti* control programs in certain areas.

Under the use of larvicides, all thirteen states reported using large quantities of oil, and eleven states reported using considerable amounts of paris green in their operations. In five states, Arkansas, Louisiana, Maryland, Mississippi and Tennessee, airplane service was used in dusting extensive areas, most of which were inaccessible or subject to excessive costs if control of the areas were attempted by other means. Only two states, Louisiana and Mississippi, reported using pyrethrum larvicide and one state, Louisiana, reported using phenol larvicide, but no indication was given as to the types of water areas on which these larvicides were used.

Inquiry was made of the various states of their blood survey work. Data which could be tabulated were received from nine states. Here again the majority of this work was done under the cooperative Malaria Control in War Areas program. The nine states reported a total of 77,011 slides examined under this program, of which 198, or 0.26 per cent, were positive. Only three states, Alabama, South Carolina and Mississippi, reported blood surveys in other than M. C. W. A. areas, in which 21,411 slides were examined. Of these, 223 or 1.04 per cent were positive. The reports of these surveys for the three states indicate generally higher rates than in the war areas. The per cent positive for each of these three groups was 0.6, 1.52 and 1.57, whereas the highest per cent positive in the war area survey groups was 0.44. Florida

reported taking many blood smears but gave no report on number of positive slides, and Tennessee reported they were cooperating with the Tennessee Valley Authority on limited house-to-house blood surveys in certain Valley areas. All but two states indicated they intended making additional blood surveys this fall.

A tabulation of personnel assigned to malaria prevention activities was requested. All thirteen states replied to this question showing a total of 98 persons assigned in the State offices and 2285 assigned to counties on operations. These figures include all classes of workers, the great majority of which were employed on activities in war areas.

Under the heading of health education people employed as malaria educators, eleven states reported a total of 77 persons assigned temporarily to this work during the summer under the M. C. W. A. program. Two states reported two persons each employed by the states as permanent employees as malaria educators. These were Texas with two full-time employees, and Florida with two educators devoting part-time to malaria education. Two states, Alabama and Maryland, reported no educators had been employed on malaria education work.

Inquiry was made as to special research work being done by the states, and three states reported such activities. Arkansas reported studying the success of vector control by insecticidal measures and the effectiveness of various insecticides. Florida reported research work on the following: (1) On splenic enlargement and associated blood findings under natural conditions; (2) Relationship of density of anopheline vector to clinical malaria as evidenced by spleen and blood survey; (3) Effectiveness of new larvicides; and (4) Effectiveness of repellents. Georgia reported carrying on observations of the efficacy of automatic siphons in controlling *Anopheles* breeding in ponds and ditches through fluctuation of pond levels and intermittent flushing of streams. They also reported that the serviceability of precast circular joint concrete ditch lining slabs and butt joint tile sub-drains in ditches was also being carefully checked.

As to financing of malaria prevention activities, the states were requested to indicate if any special funds were received for this activity, other than funds now available through the U. S. Public Health Service for Malaria Control in War Areas. No state indicated any special funds were available to them for malaria prevention, and it is assumed all such expenditures for activities other than in war areas must have been made from general appropriations.

CONCLUSION

1. From information available it appears that normal peace time malaria prevention activities of State and local health departments have been war casualties on the home front.

2. The widespread war activities in the South have, however, resulted in intensified malaria prevention activities in limited war areas.

3. In view of the above and of the history and present incidence of malaria, State Boards of Health should begin planning now to secure special funds from state, local and national official agencies for prevention of malaria on a perpetual basis. Such plans should not overlook the probabilities of the increase in the malaria hazard resulting from widespread post-war engineering projects and the feasibility of incorporating permanent malaria control on a wide basis in any post-war public works program.

4. Our men, planes and ships returning from all over the world may introduce into our midst new species of mosquitoes and more virulent parasites which would intensify our malaria problem tremendously. The armed services, the U. S. Department of Agriculture, the U. S. Public Health Service and other agencies, from scanty information available, are no doubt developing new and more effective control materials and methods which will unquestionably be of great value to states in their control efforts. It is felt the National Malaria Society should secure, analyze and pass on to State Boards of Health information of value about these new malaria preventive measures, as rapidly as the exigencies of the military forces will permit the release of such data.

COMMITTEE ON MALARIA PREVENTION ACTIVITIES

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THE INTRODUCTION OF TROPICAL DISEASES OTHER THAN MALARIA INTO THE UNITED STATES AFTER THE WAR*

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As my part in this symposium I am to discuss the introduction of tropical diseases other than malaria into this country after the war, and it has been suggested that I indicate how such introductions will affect, or should affect, the future program of the American Society of Tropical Medicine. At first glance my subject appears to be narrowly restricted. The most important disease is held out for special handling in a later symposium; only introduced tropical disease is to be considered; the time is limited to the postwar period; and the future activities proposed will be those of a non-operating scientific society. To control or eradicate introduced diseases will be the responsibility of our health authorities and the care of the sick will be provided by practicing physicians, but the Society can indirectly play a very important part in making both kinds of activity more effective and can do so in the following ways:

1. Many of its members will be taking leading parts in the control or cure of tropical diseases including those recently introduced and will be more effective because of the knowledge and advice acquired through the Society.
2. Nation-wide programs for investigation and control of introduced tropical disease could be formulated by the Society or its committees and put forward in such a way as to heighten the probability of vigorous united action on a truly scientific basis; and conversely a voice could be raised on occasion against inadequate or unscientific action.
3. The Society's greatest influence will continue to be exerted through the prompt publication of investigations by members, committees, and others in the American Journal of Tropical Medicine. This is an important safeguard against being taken by surprise by introduced tropical disease, and the influence might well be increased by the addition of an editorial section to the Journal and perhaps a department for communications.

*Read before the American Society of Tropical Medicine on November 17, 1943, at its Annual Meeting in Cincinnati, Ohio.

4. The Society can put its influence behind the movement to improve the didactic and practical teaching of tropical medicine both preventive and curative.

With these general suggestions in mind as to the mechanisms through which the Society can function effectively, we may now proceed to consider briefly several groups of diseases which might be introduced during the postwar era. The risks to be guarded against are four:

1. The introduction of diseases not now existent in the United States.
2. The introduction of new strains or types of disease organisms, which may be more dangerous than those already in the country.
3. The admission of large numbers of persons infected with disease existent in the United States with the result of wider distribution and increased incidence.
4. The introduction of the vectors of certain diseases which are presumably now absent because of the lack of their vectors.

Only a few of the diseases of especial interest in their relation to the war or the postwar period will be mentioned as examples, for more complete discussions have recently been made available by Meleney (1) and others. Since control depends so much on method of transmission, we may group these diseases on that basis.

Insect-borne Diseases

Yellow fever and dengue are two insect-borne diseases which need consideration because the common vector for both, the mosquito *Aedes aegypti*, is present in numerous places in the southern United States. Yellow fever is definitely absent from this country but exists not far away in South America and could easily be introduced by airplane by a passenger in the incubation period or by an infected mosquito were it not for the vigilance of the quarantine authorities. Dengue is possibly endemic in places in the southern states but appears more characteristically as epidemics after new introduction from near-by tropical countries or perhaps from endemic foci within our boundaries.

One thing is certain. Yellow fever will not be brought in from foreign endemic areas by our vaccinated troops, nor will they supply the fuel for outbreaks in infected countries. The postwar risk will be related to the increased civilian travel and airplane traffic, but even more to the degree to which the vector is uncontrolled within our boundaries. This highly domestic mosquito vector is

easy to exterminate locally and is not so widely distributed as generally supposed, but yet one is embarrassed to observe how in some places it is tolerated or attacked so feebly that the results are entirely inadequate. The Society might undertake to answer the following questions: Would it be worth the cost to apply against aegypti effective methods like those used in Brazil? Where should this be done? Under what centralized leadership? The situation with regard to the vector needs survey and analysis. Moreover, physicians require up-to-date and clear instructions as to methods of obtaining diagnostic proof in yellow fever cases by successive blood tests for antibodies or by the post-mortem examination of liver tissue.

Of the rickettsial insect-borne diseases we need to consider typhus fever. Our endemic murine or flea-borne typhus of the South is outside our subject. Louse-borne typhus is not likely to be introduced by troops because the present military measures for prevention include vaccination of the men exposed and keeping them free of lice. Louse-borne typhus fever was introduced by refugees from Mexico in the last World War and was widely scattered in this country without becoming established, unless in Southern California it gave rise to the present flea-borne disease (2). Now as then, the incidence of infestation with body lice is low in this country and we have little to fear. Nevertheless there exist some foci of such infestation. They should be located and completely eliminated, not only by measures to keep the population continuously louse-free through the systematic application of the newer insecticides, but also by correcting the crowding, lack of bathing facilities, and poverty, which lead to infestation. Lice are so easily transmitted through groups of people that complete eradication is the only practical policy. The Society could spread the word as to the ease with which lice may be exterminated, the methods of surveys on the basis of louse-counts, and the importance of a direct attack on the insect in discovered foci. It is doubtless worth the cost to keep communities non-infectible with louse-borne typhus while there exists a remote possibility of its introduction or of its developing from our endemic murine typhus.

Plague is endemic in rodents in a vast area of our West and is occasionally transmitted to man by their fleas. Fresh introductions would seem to be no more probable in the postwar era than at other times, and the problem of preventing rats from traveling on ships and entering our ports is receiving much attention from the quarantine authorities. This is hardly a problem specially related to the postwar era.

Filariasis due to *Filaria bancrofti* will come into the country

in military personnel from the Pacific area, but it is not expected that it will cause a serious problem here. It has doubtless been introduced frequently in the past, usually without gaining a foothold, and the fact that the disease apparently has died out in the one focus known to have been established in the United States in the early days gives us added assurance. This disease reminds us that even some of our nuisance mosquitoes, especially *Culex quinquefasciatus* of the South, may transmit disease and should not be allowed to become prevalent in our communities. If secondary cases should appear anywhere in this country, which is hardly to be expected, prompt mosquito control following adequate investigation should terminate the transmission. The real problem at present is to find an effective method of treatment for the returning infected persons, and this problem is worthy of persistent attention.

There would seem to be no serious risk of the introduction of African trypanosomiasis in the absence of its known vectors, the tsetse flies. To prevent the introduction of these insects into the Western Hemisphere, along with other disease vectors including *Anopheles gambiae* and even plant pests, the disinsectization of airplanes and ships should be effectively enforced for an indefinite time, and the influence of the Society and its members may be necessary to keep interest from waning during the postwar period. Our interest in this problem should be wide enough to cover the danger of introducing anophelines into non-malarious islands of the Pacific and into South America as well as directly into the United States.

Diseases Conveyed by Food and Water

In the postwar era cholera, bacillary dysentery, and amebic dysentery may be introduced occasionally by carriers. As the dysenteries are already here, such introductions would probably not add greatly to our general health problems. Our urban communities are becoming less infectible by these diseases as water and food supplies are rendered safer and adequate sewerage is provided. The outstanding problem is to help physicians and laboratories to become qualified in diagnosing these diseases and to supply sound advice as to the developments in chemotherapy for the dysenteries.

Diseases Due to Worms Other Than Filariasis

The danger from hookworm disease through the introduction of new infections by returning military personnel is not of sufficient importance from the community standpoint to justify numerous examinations of returning troops to detect the mild infections. *Necator*

americanus is present in certain sections of the South. *Ancylostoma duodenale* exists in parts of the American tropics and subtropics and theoretically might become established in the warmer parts of the country. In the United States, however, the degree of prevalence of hookworm disease in locations favorable to it will be determined largely by sanitation and the wearing of shoes rather than by barriers against further introduction. Primarily for the benefit of the infected individual, persons returning from endemic areas and showing unexplained anemia or other signs suggestive of hookworm disease should have their stools examined for the ova of intestinal parasites. With regard to hookworm disease the postwar problem can best be met by continuing the development of adequate health services in rural areas and by improving the teaching of diagnosis and treatment.

Schistosoma mansoni has doubtless been introduced repeatedly into the United States without becoming established. It is present in the West Indies and parts of South America, where certain indigenous species of snails have acted as intermediate hosts. These species are not present in the United States, but they have close relatives here which require investigation. Although the present knowledge is not entirely conclusive, it seems that in the absence of the known vectors the risk of the establishment in the United States of any of the species of schistosomes parasitic to man is remote, but least so in the case of *S. mansoni*. There are two measures which the Society could urge to advantage—the thorough study of the native snails that might be potential vectors until a decision as to their susceptibility is reached, and the dissemination of knowledge as to the diagnosis and treatment of these serious diseases.

From the above incomplete discussion we get certain impressions:

1. There are few tropical diseases not already in the United States which are likely to be introduced and become established in the postwar era.
2. With respect to some diseases this country is seemingly non-infectible because the necessary vectors are not here. This fact must be established experimentally, and any possible substitute vectors now in the United States should be thoroughly investigated for susceptibility.
3. Of the diseases which cannot become established, some will nevertheless be introduced and will require correct diagnosis and suitable treatment. To prevent tragedies due to diagnostic error or delay, everything possible should be done through our medical schools and through postgraduate instruction, as well as through publications in journals

and official circulars, to keep medical practitioners currently informed of the unfamiliar problems they may have to face.

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SPLEEN MEASUREMENT IN MALARIA*

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I. THE IMPORTANCE OF THE SPLEEN SURVEY

For almost a hundred years the proportion of persons in a community showing enlarged spleens and the degree of this enlargement have been used as measures of endemic malaria. When much later the parasites of malaria were discovered, microscopic examination of the blood became a routine diagnostic method, both in acute cases and for the detection of carriers. Unfortunately, in many places the latter examination alone is now carried out and provides the only data available on malaria. It is perhaps not generally recognized that the two procedures do not give the same kind of information.

The enlarged spleen is part of the general reaction of the body to repeated infections. If these infections are widely spaced, the spleen may return to normal or at least become too small to be palpated during the interval. This is the so-called hypoendemic situation which may be associated with quite an epidemic of acute cases in the summer but in which individuals on the average do not suffer from multiple and overlapping infections. The enlarged spleen is therefore an indication of the rate of transmission during the previous malaria season. But we also know that the body soon acquires an immunity to any single species or strain of plasmodium and that only mixed infections can cause a chronic splenomegaly. Since there is little cross immunity between these species and strains, each of them acts almost independently in provoking splenic reaction; and hence the chronic spleen means mixed as well as overlapping infections.

Blood examination on the other hand gives us only the number of acute cases with any accuracy and its value is greatest in epidemic situations. When it comes to identifying the apparently healthy carriers in a community, we obtain only a distant approximation of the truth. For in mixed infections, one species of plasmodium tends to dominate the picture, driving the others out of circulation; and as immunity grows, the killing mechanism of the body may suppress circulating parasites completely. We have therefore the familiar interepidemic situation of a much higher spleen

*The studies and observations on which this paper is based were conducted with the support and under the auspices of the International Health Division of The Rockefeller Foundation.

rate than parasite rate, which becomes reversed only in the presence of a seasonal wave of acute cases, or of a pronounced racial immunity.

The parasite rate therefore indicates the relative acuteness of the malaria, while the spleen rate is an index of its intensity, or in other words, of the frequency of transmission during the previous season or two. The higher the parasite rate in relation to the spleen rate, the more epidemic in character is the malaria and the lower the group immunity. The parasite rate alone therefore is not of great value in sizing up a malaria situation, but in connection with the spleen rate it affords useful information. Thus in an Italian village of the Pontine Marshes a blood examination of the population showed only 15 per cent positive. But the more complete picture is as follows:

Time:	No. Exam.	Parasites	Percent with Enlarged Spleens
Early Spring			
Children Under 12	270	33	100
Inhabitants Over 12	500	5	96

This is hyperendemic malaria, with no one escaping. But immunity and a long winter pause have reduced the parasite rate to one-third of the spleen rate in children, and the steady growth of resistance with age is shown by the fact that there were seven times as many carriers among the children as among the adults.

It is obvious that the rates will begin to drop off as soon as the season of transmission is over and the parasite rate will go down much faster than the spleen rate. Take for example two surveys in Valona (Albania):

	Parasite rate	Spleen rate
October, 1936	24	62
February, 1937	13	50

The time to determine the endemic level of malaria in a community—that is, the amount carried over from one year to the next—and to evaluate the success of control measures, is when the indices are least influenced by the seasonal wave of acute infections, namely, just before the transmission season begins. Now in areas with a low frequency of infection or a very short transmission season, the turgid spleens of acute malaria will have subsided in large part and few traces of past infection will be found either in the spleen or in the blood. This is probably why the winter or early spring survey is often neglected in this country and the returns of the diagnostic laboratory are relied upon to furnish most of the data on malaria. Even under such conditions the interseasonal spleen rate, though it may appear insignificant, is really very revealing and is the only useful basis of comparison between endemic regions.

Certainly the summer incidence of malaria fever may be very

misleading. The very mild malaria of western Spain put a third to a half of the population in bed every summer, whereas in the most malarious parts of Sardinia or the Balkans, sickness surveys showed hardly more than 2 per cent of the people down with fever at any time. But when General Sarraïl brought a French army of 100,000 men to the Balkans in 1916, 80 per cent of the force was immobilized in hospitals in a short time. Unable to draw conclusions from the statistics of acute malaria published in the United States, the League of Nations sent a commission to this country in 1927 to examine the matter. They reported that according to European standards, we had very little endemic malaria of the severe type to be found, for example, in the Mediterranean basin. It is clear that our armies of occupation and the malariologists attached to them are going to encounter in Europe conditions to which they are unaccustomed. Let us examine for a moment the findings in a Mediterranean area where malaria is fairly intense for the temperate zone, and note how the spleen survey compares with the examination of the blood in obtaining a rapid understanding of a malarious situation.

A great mass of data from both Italy and Albania is available, resulting from annual surveys made over the years by malaria services supported by the International Health Division of The Rockefeller Foundation. On the basis of an analysis by Dr. Putnam of the Foundation's statistical staff, it has been possible to summate and arrange all these data in a couple of simple tables in order to bring out certain points with respect to the spleen and blood positives. In calculating the indexes, all acute relapses with fever at the time of examination were excluded and only children between the ages of 2 and 12 were examined. In order to study the relationship between parasitemia and splenomegaly, both the blood and the spleen were examined in each individual. Some were negative (Sp. —, B1. —); some showed parasites but no spleen enlargement (Sp. —, B1. +); some had enlarged spleens but no parasites (Sp. +, B1. —); and some had both parasites and enlarged spleens (Sp. +, B1. +). All the children fell into one or another of these four classes, which could be compared both in areas where malaria was mild and where it was intense.

The following table presents such a comparison in a simplified way, revealing a number of interesting points.

TABLE I. *Data from winter surveys in seven Italian towns arranged in ascending order of spleen rates, covering 10,632 examinations over a period of 6 years (1929-1934) and showing the percentage of children in each of the four spleen-parasite classes.*

1	2	3	4	5	6	7	8	9
Spleen index group	Av. enl. spleen	Sp.— Bl.—	Sp.— Bl.+	Sp.+ Bl.—	Sp.+ Bl.+	Spleen index	Parasite index	Town
10	1.38	88	1	10	1	10.6	2.5	Portotorres
30	1.63	66	4	26	4	30.0	7.9	Sermoneta
	1.55	65	4	24	7	31.1	11.4	Siniscola
50	1.70	50	1	42	7	48.9	6.1	Ardea
90	2.14	12	1	70	17	86.5	17.5	Lodé
	2.15	9	1	70	20	90.3	20.8	Torpé
	2.35	8	1	57	34	91.0	35.1	Posada

Two things about this table strike one at first glance:

(1) Column 4 differs from the others in not being correlated in any statistical way with the spleen rate. All the other figures go up or down as the proportion and size of enlarged spleens increase, and are obviously functions of the intensity of the malaria. But the percentage of infected persons who show no enlargement of the spleen is not only relatively constant but is so small as to be almost without significance. Furthermore, this is the very group which puzzles us most since if our theories of the way the body reacts to infection are correct, it should not exist at all. The logical explanation is that the spleens of these individuals are so slightly enlarged that the examiner fails to palpate them. When we consider that the spleen must pass through a series of early stages of enlargement before it can be felt at all (and Dionisi who was a competent pathologist thought it must reach at least twice its normal size before it could be definitely palpated through the abdominal wall), this omission is no reflection on the examiner. although of course some examiners are more skilful than others in feeling small spleens. In fact, the wonder is that a much greater percentage is not missed.

(2) As a consequence of the unimportance of the "Sp.—, Bl.+" group, practically all the detectable malaria is included among the spleen positives (Column 5 and Column 6). In other words, the winter spleen survey alone in Italy revealed over 95 per cent of all the endemic malaria there was in the localities examined. It was also our most important source of information in estimating the success of control measures. We would be justified in calling it the "endemic index" had Ross not already used that term in a different sense.

To prove that this is not a phenomenon characteristic only of a certain country during certain years, I present a similar table below constructed from Albania data gathered over a different period:

TABLE II. *Data from winter surveys in 7 Albanian towns arranged in ascending order of spleen rates, covering 28,228 examinations over a period of 7 years (1932-1938) and showing the percentages of children in each of the four spleen-parasite classes.*

1	2	3	4	5	6	7	8	9
Spleen index group	Av. enl. spleen	Sp.— Bl.—	Sp.— Bl.+	Sp.+ Bl.—	Sp.+ Bl.+	Spleen index	Parasite index	Town
20	1.45	73	2	22	3	24.9	4.7	Tirana
	1.44	71	2	24	3	26.6	5.2	Durres
30	1.52	68	1	28	3	30.3	3.7	Shkoder
50	1.78	47	2	43	8	50.5	10.2	Berat
	1.81	46	3	44	7	51.5	9.8	Kavaja
	1.72	45	2	44	8	52.2	10.7	Elbasan
	1.87	41	2	49	7	56.7	9.1	Vlora

Here the towns are provincial capitals, larger than those surveyed in Italy (Table I.) and showing lower intensities of malaria on the average, although the gamut of spleen sizes is just as great. Column 4 again reveals the curiously unvarying percentage of infected persons without palpable spleens, giving the impression that it is somehow accidental and unrelated to the phenomena of malaria which we are trying to measure. The group is somewhat larger, due perhaps to less skilful examiners. This finding is undoubtedly significant because of the large numbers involved, the widely separated localities, the different insect vectors, the long period of years covering cycles of varying intensity, the number of different observers and finally the extraordinary consistency of the data. In neither table are there more than two or three figures which are noticeably out of line.

The importance of the spleen rate is obvious, although where laboratory facilities are available the parasite rate should by no means be abandoned. But the information which it gives, while valuable, is supplementary to that of the spleen survey.

II. HOW TO RECORD A SPLEEN SURVEY

There are a variety of ways of recording spleen sizes and of arriving at the spleen index of a community, as the League of Nations Committee discovered in 1938 when it met to draw up a report on "Terminology in Malaria." That report, published in the *Bulletin of the Health Organisation of the League*, Vol. 9, No. 2, 1940, does not attempt to pronounce in favor of one system over another. This paper on the other hand is presented

for the express purpose of suggesting a standard procedure which if generally adopted would make reports of spleen surveys understandable to all and would permit comparisons to be drawn between one region and another. It is not a new method, for with unimportant variations it is now in use in many countries, notably the Mediterranean basin, the Near East, Russia, India and South America. It has not been adopted by the French "paludologues" nor in general in North America. It is not the invention of any one person but represents an evolution through years of experimentation and confabulation. I consider it an improvement on methods which I have previously advocated, and which assiduous authors still rake up from the old publications and label with my name. In general the process has been one of simplification involving fewer classes of spleen, a more restricted age group, the dropping of decimal places and the attempt to reach in a single figure (the average enlarged spleen) a useful and reasonably faithful expression of the intensity of malaria in a community.

1. *Terminology.* There has been much debate about the use of the words "rate" and "index". In my opinion, what we are obtaining is the *spleen rate* of the group we are examining which at the same time is the *spleen index* of the whole community

2. *The Standard Age Group.* The unqualified term "spleen rate" should be restricted to young children. Older persons ought at times to be examined; but the result should be labeled "adult spleen rate" or otherwise described, and the data kept distinct from the standard spleen rate as generally accepted and used for comparison. There is an excellent reason for this. The rates are usually very different in children and adults and, therefore, mean nothing when averaged. Under conditions of intense transmission (as in West Africa) the rate in children under 10 may be 100 per cent, while that of adults, through the development of a solid immunity in those who survive, may decline to a very low level approaching zero. We should therefore limit the age group examined to that which shows the least effects of immunity. It has been found that the age group 2-9 is the most constant as to spleen rate, and this is the group routinely surveyed in India and Africa where malaria is exceedingly intense. In the next age group (10-14) the spleen rate is often considerably reduced, while babies (0-1) are difficult to examine and have soft, acute spleens if they show any enlargement at all. In practice, however, children are most often contacted in schools for such surveys, in spite of certain theoretical objections to this procedure, and the preschool children (2-5) are not included in representative numbers. In areas where group immunity is

less early developed, the age group under examination could be extended to 12 or even 14 years without seriously affecting the result. It would be desirable therefore *if the standard spleen rate were understood to refer to children in this relatively non-immune period, excluding babies.*¹

3. *Measuring Splenic Enlargement.* We cannot measure directly the volume or mass of the spleen, and the most practical alternative is to determine how far the spleen projects below the costal margin by noting on the abdomen the position of the lower edge (not the apex). It is recommended that the child be examined lying on his back with knees flexed, although in India he is usually examined standing. It is also recommended that the *point of furthest projection of the spleen downwards into the abdomen* be recorded rather than the position of the apex. The weight of the growing spleen causes it to sag toward the left side of the abdomen as it descends, so that the lowest point follows a line running from the point of emergence at the costal margin roughly straight downwards into the left iliac fossa.

Authoritative authors like Christophers, Boyd and Russell prefer to locate the apex, and since this is pushed more and more toward the right side of the body as the spleen grows larger, they measure the projection of the spleen not straight downward but along an oblique line drawn from the supposed position of the apex of the normal spleen to the symphysis pubis (Boyd) or through the umbilicus (Christophers, Russell). This method is theoretically sound, but is little followed in practice since most doctors, in the desire to examine the largest number of children in the shortest possible time, feel for the lower border rather than the apex, which is often troublesome to locate. This introduces little error since the measurements are made along different radii of the same circle, and the intrinsic roughness of the whole procedure makes any small discrepancies insignificant.

4. *Recording Spleen Sizes.* Christophers (1) uses a tape measure and records in centimeters the distance of the apex of the enlarged spleen from the costal margin or the umbilicus. Since this does not take into account the size of the child, the figures have to be reduced by means of a table to those corresponding to a "standard" child of a sitting height of 60 centimeters. If the object of the survey is a scientific study of the effects of malaria on the

¹It is of course also of interest in any malarious community to determine the average age at which the spleen rate begins to fall off, since this is one of the best indications we have of the local intensity of transmission over the years. Under purely epidemic conditions, children and adults will have the same spleen rate.

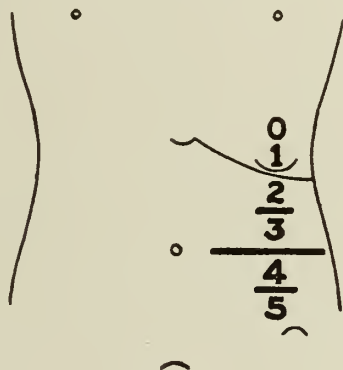
spleen, then such accuracy is not only desirable but necessary. But where the average splenic enlargement is being estimated as a rough and ready indication of malaria intensity in a community, then something much more simple will suffice.

Schüffner (2) suggested the most practical method, namely, to subdivide the abdominal surface to the left of the midline into equal numbered spaces from the costal margin to the symphysis pubis, and simply record the number of the space into which the lower border of the spleen projects. Schüffner proposed a considerable number of subdivisions (eight in all) but experience soon showed that this was too many; and in my early work in Italy I reduced the number to six. This was a mistake, since the results were incommensurable with those obtained before and there were still too many spleen sizes, so that the present scheme was finally adopted of having only two spaces above and two below the level of the umbilicus. This gives four classes of spleen below the costal margin, which have proved to be ample for all practical purposes. This is now generally accepted.

The greatest difference of opinion centers about the very small spleens palpable at or above the costal margin. Years ago they were considered of little importance and generally ignored, as indeed is apt to be the case still, where malaria is intense. Darling first pointed out their significance in this country and Paul Russell has argued that they are sometimes the most important part of the picture. Most of these slightly enlarged spleens can only be palpated when the patient forces the spleen downward by a deep inspiration; and there are treshold spleens which can be felt only in lean individuals or by very experienced examiners. When this group was grudgingly admitted to classification, it was kept in a different category from the rest and was not referred to by number. Thus Boyd (3), following Darling, designates spleens which can be felt only with the assistance of the patient, as "PDI" (palpable on deep inspiration), and Russell calls them "PI" spleens but considers that they are already approximately twice the volume of normal spleens and hence of equal importance to those projecting into the numbered spaces of the abdomen. I thoroughly agree with this opinion but I believe that if they are to be given their true value and taken into consideration in calculating the "average enlarged spleen" of a group, they should be assigned a number for the sake of simplicity and statistical manipulation. In fact, enlarged spleens which can be felt only when the patient takes a deep breath are now classed

as No. 1 spleens by many observers, and it is suggested that this be made the general practice.²

The scheme proposed, then, is to make one group of all those small spleens which can only be felt with the assistance of the patient and which project into the space which is covered by the ribs between the normal spleen and the costal margin. These PDI or PI spleens are given the number 1, and the larger spleens are numbered in succession 2 and 3 if above the level of the umbilicus or 4 and 5 if below it. There are two obvious advantages to this simple scheme. It provides an objective line of separation between spleens just above and just below the costal margin, and all spleen classes are given numbers by which they can be "weighted" in determining the average enlarged spleen of a group of people. The frame of measurement is as follows:



In the above figure:

0=normal or non-palpated spleen ("negative" spleen).

1=spleen palpable only when the subject draws a deep breath.

2=spleens ranging from those at the costal margin palpable without assistance from the subject to those whose lower border reaches a point halfway to a horizontal line through the umbilicus.

3=spleens projecting more than halfway to the umbilical level but not beyond it.

4=spleens below the umbilical level but not more than halfway to the line of the symphysis pubis.

5=all spleens larger than those mentioned above.

5. *Importance of the Average Enlarged Spleen.* We are interested not only in the crude spleen rate—the percentage of children showing palpable enlargement of the spleen—but also in the

²Boyd assigns No. 1 to spleens at the costal margin which are just palpable without deep breathing. I would classify these as No. 2 spleens.

"average enlarged spleen" which is the mean linear projection of the spleen in the group of spleen positives. The two figures tell us how many in the community have palpable spleens, and how large these spleens are on the average. They are really unrelated values since each may vary independently of the other. One species or strain of parasite may enlarge the spleen more than another (as Barber concluded in Egypt) so that two communities might have the same spleen index but a different average spleen size. The variety of species and strains present in a locality will have the same influence since the spleen reacts to each as to a new infection, there being little cross immunity. More important is the length of the transmission season. Dr. H. P. Carr and I examined the pupils of a small rural school in Peru in the winter, finding a spleen rate of 63 (a hyperendemic figure) but an average enlarged spleen of hardly more than 1 (most of the spleens were only just palpable). This was interpreted to mean a very short, intense period of infection in summer. Swellengrebel mentions the island of Modjowarno near Java, where transmission is restricted to one month a year. The spleen rate is usually 50 per cent or more in the off-season, but the spleens tend to disappear entirely before the next annual epidemic wave. With longer transmission seasons the average enlarged spleen increases with the spleen rate, as can be seen in Tables I and II.

The "average spleen" is less important since it is influenced by both the spleen rate and the spleen size. Its interpretation depends on knowing the other data, since the same average spleen may result from two different situations, in one of which the spleens are larger, and in the other the spleen rate is higher. It is therefore a derived, as distinguished from an independent, value and can be calculated from the spleen rate and the average enlarged spleen, as shown below.

6. *Calculation of the Spleen Rate (S), the Average Enlarged Spleen (AES), and the Average Spleen (A).* Striking an average is simple since we are dealing not with spleen volumes or masses at which we can only guess, but with linear measurements on a surface. The numbers given to the different spleen groups are units of measurement applied to their linear projections into the abdomen. The number assigned by the examiner to each spleen is therefore the factor needed to give that spleen its proper weighting

in the general average. This is shown in the example below:

Position and weighting of spleen		No. of children examined		No. of spleens multiplied by weighting	
0	×	40	=	0	
1	×	20	=	20	
2	×	25	=	50	
3	×	10	=	30	
4	×	4	=	16	
5	×	1	=	5	
No. of enlarged spleens:		60	into	121	= 2.0
Total number examined:		100	therefore	60/100	= 60%
AES	×	S	= 2.0	×	.60 = 1.2

positive of the average enlarged spleen (AES)
the spleen rate (S)
position of the average spleen (A)

This method of calculation is in line with the recommendations of the League of Nations Committee on Terminology and is simpler and more logical than that of Boyd or Russell, or the older method previously advocated by myself (4). These methods assigned a weighting of "1" to negative spleens instead of "0" as above. This was not correct, for we are dealing with linear distances from a fixed point (the lower border of the normal spleen) and not with masses or volumes. If we were comparing volumes, the unit volume (in this case the normal spleen) would be correctly taken as "1," but distances are always measured from zero as a starting point (see the scale on any map). The older method arrived at the same result in the end, but by a roundabout process, for since the weighting for each spleen class was greater by 1 than its position, 1 had to be subtracted from the answer to find the position of the average spleen and average enlarged spleen. The method given in the above example, by making the weighting and the position identical, gives the correct mean projection of the enlarged spleens at once without any decoding.

DISCUSSION

The method of recording and averaging spleen sizes which has been described above is, with certain local modifications, standard practice in many parts of the world. It has been criticized as inexact, but if I have frequently used the words "roughly" and "approximately" in this paper, it has not been to forestall the objections of perfectionists but because the estimation of the degree of splenic enlargement by palpation through the abdominal wall is in fact a rough and ready procedure. Considering that some spleens are long and some globular, that some belly walls are thick and others thin, that costal margins take on curious slants and ab-

normalities and that children come in various shapes and sizes, it is clear that "estimate" is the proper word rather than "measurement." The way to correct errors introduced by individual peculiarities is not to insist on a more elaborate description but to examine large numbers of individuals and thus swamp the eccentricities.

The fact that a spleen survey gives more information about an unknown endemic situation than a blood survey and gives it more quickly and easily does not mean that microscopic examination of blood preparations should be neglected. It is always good practice to do both where facilities are available. They present different pictures of the same situation and reinforce each other when the results are analyzed. The spleen and blood examination should always be made on the same individuals so that the results can be tabulated in the following concise and adequate form:

TABLE III. Spleen and blood survey of Valona (Albania), February, 1937

Parasites	Spleens: Neg.	1	2	3	4	5	Total parasites
Neg.	246	89	78	17	4	1	435
F.	2	6	19	6	0	0	33
V.	9	3	7	2	0	0	21
M.	1	2	6	2	0	0	11
Total spleens: 258	100	110	27	4	1		500

} blood positive
65

Spleen positive: 242

Spleen rate	242/500	×	100	=	48
Parasite rate	65/500	×	100	=	13
Average enlarged spleen	422/242	=			1.7
Average spleen	422/500	=			0.8

(Note: Rates are reported as whole numbers, averages are carried out to one decimal place. The utility of examining an even hundred children, or some multiple, is evident in analyzing results.)

Provided with tables like the one above, covering a period of years, biometricians have the necessary data with which to analyze the nature and time trend of the relationship between blood and spleen findings, and to study the significance of the enlarged spleen in malarious zones.

Summary

Analysis of the data gathered in the examination of some 40,000 individuals for enlarged spleens and malaria parasites in Italy and Albania over a period of years discloses some interesting facts as to the relative importance of spleen and blood findings in sizing up an endemic situation. Over 95 per cent of the endemic malaria present was revealed by the spleen survey alone. The importance of the spleen survey is such, both in evaluating the results of control measures from year to year and in comparing one area with another as to malaria intensity, that acceptance of a standard method of examining spleens and recording their sizes would mark a great advance in the investigation of malaria and in our ability to interpret the observations of others as reported from all over the world. A simplified method is described which has stood the test of time and of statisticians in many lands.

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NOTES ON THE CONSTRUCTION AND USE OF STABLE TRAPS FOR MOSQUITO STUDIES¹

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Introduction

When we started a study of anophelines and malaria in Egypt, it became apparent that one of the first requirements was a method of trapping mosquitoes. Of the four species of *Anopheles* found in the Egyptian Delta only *sergenti* could be collected regularly in houses or stables, and this in relatively small numbers. *A. pharoensis*, the predominant species of the Delta, was almost never found resting in buildings, though it could be collected in large numbers by sweeping in the rice fields with an insect net. *A. coustani* was occasionally caught biting man, but never found resting in houses. *A. multicolor* was very common, judging by the number of larvae; yet during a year of collecting only about 25 adult mosquitoes were found in searching dwellings and other buildings. A stable trap exactly like that described by Magoon (1935) was built, but very few mosquitoes were caught. Many mosquitoes apparently managed to escape from the trap, as the number caught was increased considerably when the ingress slits of the trap were closed before daylight. This was an awkward expedient, however, as it required that a man with an alarm clock sleep near the trap.

We started experiments with trap construction in the spring of 1940, but the progress of the war made it advisable to suspend the work before the experiments had progressed very far. We did, however, succeed in designing a trap that seemed to be successful under Egyptian conditions, as we were able to collect four or five thousand mosquitoes per trap night, including as many as a thousand anophelines. A trap similar to the Egyptian model was constructed in Colombia, for use in connection with the mosquito studies being carried out in the region of Villavicencio. This trap has proved satisfactory under Colombian conditions. Stable traps offer great promise as a method of checking on anopheline or other mosquito abundance, and as a tool for studies of mosquito behavior.

¹ The studies and observations on which this paper is based were conducted with the support and under the auspices of the Section of Special Studies maintained by the Colombian Government and the International Health Division of The Rockefeller Foundation.

It may consequently be worth while to describe the methods of design that we developed in Egypt and to give the results of experiments made in Colombia. Considerable improvements in design could no doubt be made by further experimentation, and it is in the hope of stimulating such work that these notes are published.

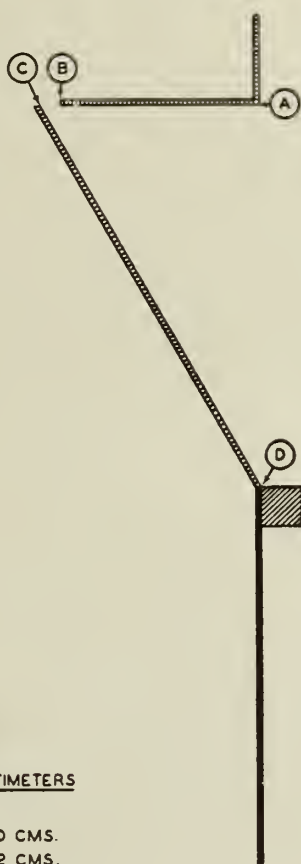
It is very convenient to have a name for a particular type of trap, and it is customary to use a personal name such as "Magoon Trap" or "Shannon Trap." This system is perhaps somewhat unfair, as a particular apparatus usually represents an accumulation of ideas from many sources. The trap described by Magoon includes ideas contributed by Earle. The trap described here stems, of course, from that developed by Magoon, with further contributions from Dr. L. W. Hackett, Dr. Henry W. Kumm, and various carpenters and technicians. In view of this it would seem best to refer to the former trap as the "Caribbean trap," since it was developed and has been extensively used in the Caribbean area; and to refer to the trap described in the present paper as the "Egyptian trap," since it was first developed in response to the particular problems of that fauna.

Trap Construction

Ingress baffle. The fact that in Egypt it was necessary to close the ingress slits of the Caribbean trap in order to catch anophelines showed that the main difficulty with the trap was in the construction of the baffle. It has frequently been observed in the laboratory that anophelines, in attempting to escape from an enclosure, tend to make flights varying from upward to horizontal in direction; they rarely fly downward except in response to a definite stimulus, and even a phototropic reaction is greatly inhibited when the source of light is below the mosquito. We have consequently experimented with ingress baffles with the opening in a horizontal plane. The design of the baffle that has proven successful in Egypt and Colombia is shown in figure 1. The opening is placed at some distance in from the side of the cage in order to prevent the accidental escape of mosquitoes flying against the sides; since the mosquitoes might be attracted to the opening if it were conspicuously lighter than the sides of the baffle, these have been made of transparent material instead of boards. The basic principle of the horizontal ingress slit in mosquito traps has been described by van Thiel (1939). Colonel W. H. W. Komp informs me that stable traps with this type of baffle were used successfully in Panama some years ago. The principle is also embodied in the netting trap described by Shannon (1939).

Our experiments with trap construction were carried out in Egypt, and it seemed desirable to make comparative tests of horizontal and vertical baffles with neotropical mosquitoes to see whether there would be a significant difference in catch in that fauna also. Two traps, identical except for the ingress baffle, were run in

INGRESS BAFFLE OF EGYPTIAN TRAP TO SHOW HORIZONTAL OPENING



MEASUREMENTS IN CENTIMETERS

A TO B	=	20 CMS.
B TO C	=	2 CMS.
C TO D	=	44 CMS.
A TO D	=	38 CMS.

..... = SCREEN

———— = SHEET IRON OR PLYWOOD

FIGURE 1

parallel near Villavicencio, Colombia, with the results summarized in Table 1. Trap "A" was built with ingress baffles, exactly as described by Magoon (1935), on all four sides of the trap; trap "B" had horizontal baffles on the two sides, as shown in Figure 1 and in the photograph, Figure 2, with no openings at the ends. The traps



Fig. 2. Trap with horizontal baffles on two sides and no openings at the ends

were alternated in position, and the two donkeys used for bait were alternated in the traps. The results seem to show that the horizontal opening is definitely superior in this fauna also.

Materials and Construction. We have built traps of various sizes, depending on the use for which they were intended, but we have recently standardized our dimensions, making all traps 2 meters long, 1 meter wide, and 1.75 meters high. This size is large enough to hold a man, lying prone on a cot, and it is also convenient for a donkey. Smaller traps can be used when the bait is sheep, calf, or pig, but it seems better to use a uniform size if comparisons are to be made between trap captures with different baits. The accompanying photograph is intended to give an idea of the general construction and appearance of the trap.

The lower meter of the trap, on all four sides, is closed with either wood, plywood, or galvanized iron. The upper part of the trap is screened. We use an aluminum alloy screening which is very satisfactory because of its durability and light color (great trans-

parency), but other types of metal screening seem to be equally good. A trap with aluminum screening gave a much better catch than a similar trap with cloth netting in a series of trials in Egypt, the differences being probably due to the lessened contrast of the slit of the ingress baffle.

Both laboratory and field observations showed that all four species of the Egyptian anophelines tended to fly into the open in the early morning, rather than into dark corners of an enclosure (cage, house, stable). Consequently we thought that our trap might be more successful if it were made with a transparent roof so that enclosed mosquitoes would tend to be attracted upward, away from the ingress baffle. The first trap was built with a roof of cloth netting (this was in rainless country) and a piece of Celotex was cut that could be fitted over this so that the trials could be made with the top either open or closed. The first trials showed that the type of roof covering had no influence on the captures, and all of the subsequent studies in Egypt were made with traps with solid roofs. In Colombia we have built all of our traps with transparent roofs, using a cellophane-filled aluminum screening sold under the trade name of "Vimlite." This material is strong, light, and remains waterproof under tropical rain forest conditions for a year. It is a very convenient material for such purposes, even though a transparent roof is not necessary.

The details of the construction of a dismountable trap are given by Magoon. Every good laboratory carpenter will probably develop slightly different methods of construction, so that there is little point in giving minute specifications. Details of construction depend on the materials available, on the animal to be used as bait, and on the degree of portability required. Where traps have to be carried by man-power into the forest, we have found that the sides can be built of two sections (instead of one) and the trap still be sturdy enough for most purposes. Where a donkey or calf is to be used for bait, it is advisable to build doors in both ends of the trap, so that the animal can enter at one end and be taken out at the other: an improvement first tried out by Dr. Kumm in connection with his studies in El Salvador.

We find it convenient, in Colombia, to build a cement platform surrounded by a shallow moat with water in a location where a trap is to be used for any length of time. The moat prevents the entrance of ants, which may be very destructive, and the cement floor makes the trap easier to keep clean. Such a platform and moat are particularly necessary when the trap is to be used in the forest.

In temporary locations it is often useful to make a wooden floor for the trap.

Host Preference Studies

Stable traps have been largely used as a method of checking on the efficiency of mosquito control measures (Earle and Howard, 1936). They would seem also to be well adapted to the study of certain aspects of mosquito biology. Captures with standard traps and standard baits can be used for studying the relative density of mosquito populations in different times and places, *i. e.*, for studies of local and seasonal distribution. Parallel captures with standard traps and different baits would seem to be an ideal method of studying mosquito host preference.

Host preference studies have generally been carried out either by the precipitin method (Rice and Barber, 1935), or by observations on caged mosquitoes (van Thiel, 1939). Precipitin tests always show a bias depending on the place where the mosquitoes were collected (house, stable), and the method can in any event only be applied to mosquitoes that rest in places where they can be caught while containing fresh blood. The cage method of study is relatively cumbersome, requiring the breeding of large numbers of mosquitoes, and it is always open to some question because of the possible abnormal behavior of caged mosquitoes, particularly when these are unfertilized.

A short series of tests made in the vicinity of Cairo, Egypt, is summarized in Table II to show how the trap method could be used in making host preference studies. The difference in attractiveness between individual animals of the same species may be large, and a series of observations with several individuals of each host species would be necessary before one could draw valid conclusions about specific differences. The possible extent of individual differences is shown by the catches with two donkeys summarized in Table I. Both animals were young, but donkey "M" (a considerably larger animal) was almost three times as attractive as donkey "C."

Studies of Seasonal Distribution

Stable traps would seem also to furnish a very good method for the study of seasonal distribution of mosquitoes. The possibilities of the method are shown by the studies of Kumm and Zúñiga (1944) in El Salvador. We have made regular collections in one trap in the vicinity of Villavicencio for over two years, and the data of the captures of *Anopheles rangeli* and *Psorophora cingulata* for

the calendar year 1942 are summarized in Figure 3 as another illustration of the stable trap method of study. The figures for *Anopheles rangeli* are approximate, as it is difficult to identify this species on adult female characters alone. The eggs are very distinctive, and by

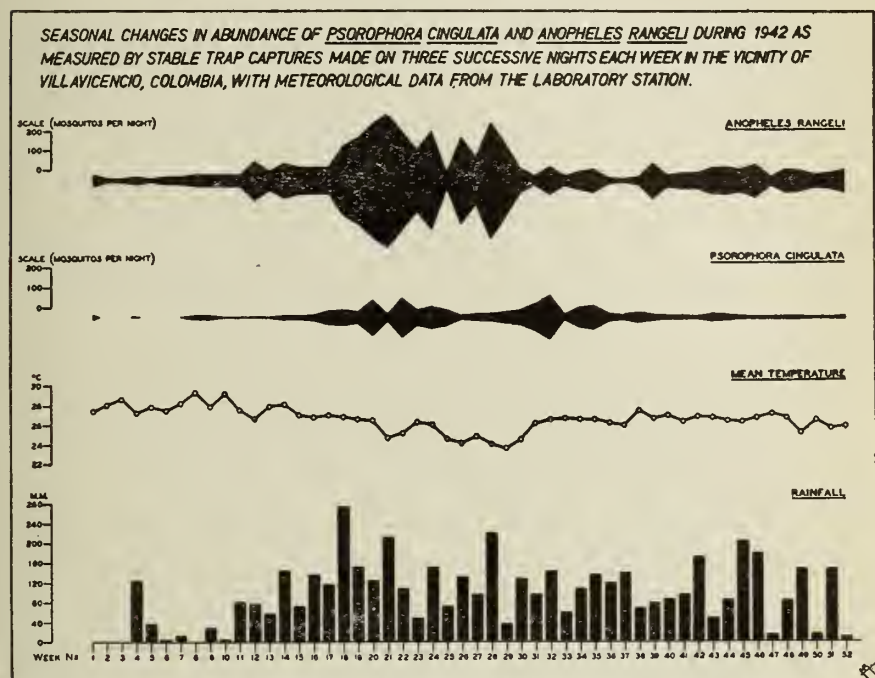


Fig. 3

the examination of occasional series of egg batches we have found that 90 to 100 per cent of the *Nyssorhynchus* with *rangeli* tarsal markings are of this species, the remainder being *triannulatus*. This slight admixture of *triannulatus* does not affect the general trend of the *rangeli* seasonal curve.

The data on which the graph is based were obtained by running the stable trap on Sunday, Monday, and Tuesday nights of each week. The trap was in the same location, and the same donkey was used as bait, throughout the year. The weekly capture rate was determined by averaging the three catches. We ran the trap on this schedule partly for convenience and partly in order to get data on the results of successive catches. Gabaldon and co-workers (1940) found that "a baited stable trap in one location caught more anophelines the first night than it did the second and third." They

could get a "first night" type of catch by moving the trap to a new location only three meters away. They did this repeatedly and their figures leave no doubt but what a slight change in the position of a trap has great influence on the relative catch. The results of 54 three-night runs of our trap are summarized in Table III from this point of view. The first of the three nights had the largest catch in 35 of the 54 weeks; the catches on the second and third nights showed less difference than that found by Gabaldon, and the difference might be ascribed to chance. Our figures might well be explained by "catching out," but no such explanation is possible in the case of Gabaldon's results where the trap was moved only three meters. This is a factor that must be taken into account in arranging studies with stable traps, but it does not by any means invalidate their usefulness.

The data in the accompanying graph are intended to illustrate the use of stable traps rather than the seasonal distribution of eastern Colombian mosquitoes, as it would be somewhat hazardous to base generalizations on observations during a single year. It is nevertheless interesting that the dry season (weeks 1 to 13) seems to be the controlling factor in mosquito abundance. *Anopheles rangeli* stays at a low and fairly uniform level, while *Psorophora cingulata* (like other species that breed in transient pools and that are able to aestivate in the egg stage) disappears altogether. Almost all of the local mosquito populations seem to build up to a peak of abundance after the dry season, this peak usually falling in May or June, and then to decline in numbers. This seems curious, as environmental conditions remain fairly constant; possibly it is due to the development for a host-predator cycle or some similar phenomenon.

Summary

Anophelines with outdoor resting habits are apparently able to escape from traps with a vertical opening rather readily; it was found that mosquitoes that could not be caught in numbers in stable traps with the ordinary vertical ingress slit could be trapped if this ingress were arranged in the horizontal plane so that the mosquitoes would have to fly downwards to escape. The catch was also increased if the ingress baffle was made of wire netting stretched taut so that wooden supports, which served to make the opening more conspicuous, were not needed. The catch is apparently about the same whether the roof is made of transparent or opaque materials.

The possibility of using stable traps for studies of host prefer-

ence and of seasonal distribution is discussed, with examples from experience in Egypt and Colombia.

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Parallel mosquito catches with Caribbean trap (A) and Egyptian trap (B) in the vicinity of Villavicencio, Colombia.

TABLE I.

Date	Trap	Bait (donkey)	Total Mosqui- toes	<i>Anopheles</i>	<i>Culex</i>	<i>Mansonia</i>	<i>Psorophora</i> <i>cingulata</i>
14-VII	B	M	82	23	29	26	4
14-VII	A	C	15	2	0	13	0
15-VII	B	C	72	20	42	0	10
15-VII	A	M	37	8	0	27	2
16-VII	B	M	102	27	51	5	19
16-VII	A	C	6	3	0	3	0
(Positions of Traps Reversed):							
20-VII	B	M	140	55	31	9	45
20-VII	A	C	9	4	0	5	0
21-VII	B	C	43	11	19	2	11
21-VII	A	M	9	2	1	6	0
22-VII	B	M	47	6	28	3	10
22-VII	A	C	2	0	0	2	0
23-VII	B	C	16	0	8	0	8
23-VII	A	M	0	0	0	0	0

Average catch per night:

Trap	Total	<i>Anopheles</i>	<i>Culex</i>	<i>Mansonia</i>	<i>Psorophora</i>
Caribbean (A)	10.3	2.7	0.1	8.0	9.3
Egyptian (B)	73.6	20.3	29.7	6.4	15.3

Difference between donkeys:

Average catch per night with donkey "M":	61.1 mosquitoes
donkey "C":	23.7 mosquitoes
donkey "M" in Caribbean trap:	15 mosquitoes
donkey "M" in Egyptian trap :	96 mosquitoes
donkey "C" in Caribbean trap:	8 mosquitoes
donkey "C" in Egyptian trap :	44 mosquitoes

TABLE II.

Trials with different animals as bait in stable traps near Cairo, Egypt:

Date	Trap	Bait	Anophelines Caught	
			<i>A. pharoensis</i>	<i>A. multicolor</i>
4-VI	B	Calf	148	55
4-VI	D	Donkey	170	42
5-VI	B	Donkey	235	54
5-VI	D	Calf	825	62
6-VI	B	Calf	710	42
6-VI	D	Sheep	70	10
7-VI	B	Sheep	320	15
7-VI	D	Calf	820	42

Summary: Mosquitoes per trial with

	Calf	Donkey	Sheep	Trap B	Trap D
<i>A. pharoensis</i>	626	202	195	353	471
<i>A. multicolor</i>	50	48	12	42	39

TABLE III.

Results of three successive nightly runs with a stable trap in a fixed location during fifty-four weeks: relative position of runs based on total mosquito catch.

Number of times:	Position of Catch		
	First	Second	Third
First night	35	14	5
Second night	12	21	21
Third night	7	19	28

TABLE IV.

Supporting data for graph of seasonal distribution of mosquitoes in the vicinity of Villavicencio during 1942 (Fig. 3):

Week no.	Rainfall mm.	Mean temperature	Mean of captures in stable trap	
			<i>Anopheles rangeli</i>	<i>Psorophora cingulata</i>
1	0.0	27.5	54	7
2	0.0	28.0	15	0
3	0.0	28.6	21	0
4	124.5	27.1	30	1
5	36.5	27.8	19	0
6	1.0	27.4	30	0
7	9.5	28.2	25	1
8	0.0	29.1	62	6
9	29.5	27.9	60	9
10	2.5	29.2	58	2
11	81.5	27.5	64	1
12	77.5	26.7	209	3
13	56.0	27.9	107	2
14	183.0	28.0	173	7
15	73.5	27.0	134	14
16	136.0	26.8	144	38
17	96.0	27.0	135	78
18	273.0	26.8	379	87
19	149.5	26.6	442	78
20	125.0	26.5	575	213
21	214.0	24.7	687	47
22	104.5	25.1	500	231
23	49.5	26.3	330	114
24	152.0	26.0	494	126
25	74.5	24.6	91	102
26	134.0	24.2	428	22
27	96.0	24.9	248	42
28	222.0	24.1	592	51
29	35.0	23.7	376	82
30	128.5	24.6	135	89
31	96.5	26.2	52	164
32	143.5	25.5	136	272
33	61.0	26.6	53	32
34	108.0	26.5	96	94
35	137.0	26.5	119	127
36	118.5	26.1	22	36
37	139.0	25.9	17	12
38	68.5	27.5	34	55
39	78.5	26.6	192	34
40	86.0	27.0	61	10
41	97.0	26.3	83	12
42	172.5	26.8	80	14
43	47.0	26.7	137	37
44	83.0	26.5	138	28
45	203.5	26.4	127	14
46	181.0	26.8	174	16
47	13.5	27.1	57	9
48	84.0	26.9	122	17
49	147.5	25.3	110	7
50	15.5	26.5	70	4
51	148.0	25.9	77	5
52	7.5	26.0	65	12

REPORT ON MALARIA TERMINOLOGY FROM THE COMMITTEE ON MEDICAL RESEARCH

In the field of malaria, there is a lack of uniformity in terminology. Because of this, some writers have failed to impart an exact impression of their observations or have failed to designate the species of malaria on which they were working.

Many of the important reports on malaria in this country originate from members of the National Malaria Society. Should the Society agree upon and adopt a definite terminology, such a move would undoubtedly be a tremendous step toward uniformity.

The need for such a step has been recognized and variously suggested. The American Journal of Public Health in July, 1943, carried an editorial on the subject. Dr. M. F. Boyd in the "Symposium on Human Malaria" suggested, as have others, the desirability of using specific terms for the various malaria infections. The Health Organization of the League of Nations in its Bulletin, Vol. IX, No. 2, 1940, published a Report on Terminology in Malaria in which desirable terms were suggested.

The Committee therefore respectfully suggests that the Society take steps to draw up and adopt a uniform terminology in malaria. Inasmuch as most of the basic terms are considered in the above mentioned Report of the League of Nations Health Organization, this report might well be used as a basis. The terms in this Report with which disagreements are found could be indicated and better terms suggested.

As an example of the standardization process, the following examples are offered:

1. The term, malaria, should be modified by the specific name of the etiological agent instead of the colloquial name, viz.: Infections of *Plasmodium falciparum* should be designated as *falciparum* malaria instead of as malignant tertian, estivo autumnal, tropical, subtertian, pernicious malaria, etc.
2. Parasitic and clinical periods of the infections should be differentiated. The parasitic periods should be designated prepatent, patent and subpatent and the clinical periods should be designated incubation, symptomatic and latent (?).
3. Definition of induced malaria, as in the treatment of neurosyphilitics, should be designated "malaria experimentally contracted" and should be divided into two types:
(a) Blood-induced.

(b) Sporozoite-induced.

This more precise phraseology is suggested as better than "artificially induced."

As a result of the above report and at the suggestion of the Chairman of the Committee on Medical Research, the Society voted to approve the preparation of a report on a uniform terminology in malaria and to instruct the incoming President to appoint a committee to prepare such a report. In discussing this motion the Chairman of the Committee on Medical Research pointed out that it was very desirable that the chairman and members of such a committee should be fundamentally interested in terminology. The present report of the Committee was prepared by Dr. Martin D. Young, but he feels unable to continue work on the subject because of the press of present duties in the U. S. Public Health Service.

STATEMENT FOR THE NATIONAL MALARIA SOCIETY

(Submitted for inclusion in Report of the Committee on Malaria Prevention at the meeting in Cincinnati, Ohio, November 16-18, 1943)

During the season of 1943, the Tennessee Valley Authority had under operation eight main river reservoirs with a total shoreline of approximately 4,700 miles, and twelve tributary reservoirs with a total shoreline of about 2,100 miles; a grand total of 6,800 miles of shoreline. One of the main river reservoirs, Fort Loudon, was impounded in the late summer. A tributary reservoir, Douglas, was filled in the early spring of 1943.

The work has been handicapped seriously here, as elsewhere, by difficulty in securing personnel, materials, and supplies and by restrictions on use of tires and gasoline.

OPERATIONS PROGRAM

The usual anti-larval program was carried out, consisting of removal of vegetation from the zone of fluctuation during the fall and winter, together with the use of the flood surcharge zone in the spring for stranding driftage and floatage, inclusion of a constant pool level phase in the early growing season, seasonal recession of peak elevation combined with cyclical fluctuation of water level. Larvicides continued to be used in areas where naturalistic measures required supplementation.

As has been previously reported, mosquito proofing of houses in lieu of the application of larvicides has been the method of con-

trol in some sections of the Wheeler reservoir. A mosquito-proofing program is proposed in three areas in the Guntersville reservoir but has been delayed because of difficulty in securing material, but it is expected that this will be secured in time for the work to be started during the winter.

Schedules for water level control on TVA reservoirs were developed on the basis of a general pattern for the system for the entire mosquito-breeding season rather than on an individual reservoir basis. This will be discussed in a paper presented at this meeting by A. D. Hess and C. C. Kiker. In general, the schedules of reservoir operation were the most favorable for malaria control which have been experienced. Due to stream flow conditions, the operations of the main river reservoirs were quite favorable. The tributary reservoirs which were all filled by the early part of the season were drawn upon to give a recession which controlled anopheline production, with application of larvicides necessary in only one reservoir.

In the Kentucky reservoir, which will be impounded in 1944, eight diking and dewatering projects are under construction. Nine areas are proposed for deepening and filling. These permanent shoreline improvements will be discussed in a paper to be presented at this meeting by Dr. E. L. Bishop and Mr. F. E. Gartrell.

Arrangements have been completed for the inauguration of a program of land-use restriction to daytime occupancy in certain areas bordering the Kentucky reservoir where mosquito-control measures are likely to be less effective. The land in those areas is of relatively low agricultural value and is bordered by localities of sparse population.

RESEARCH PROGRAM

The following are some of the accomplishments of malaria-control investigation during the past season:

1. Detailed studies on the water-level relationships of plant phenology to water-level management for malaria control emphasize the importance of a relatively constant pool level phase in the early spring and the limiting of seasonal recession to the amount required for current mosquito control in order to limit the invasion of marginal vegetation into the zone of fluctuation.
2. Investigations of the relative effectiveness of various types of shoreline conditioning measures show that major benefits are received from the annual rebrushing operations in the zone of fluctuation.

3. Studies on the intersection line indicate that it is probably the most important single determining factor in the production of malaria mosquitoes in the reservoirs of the Authority. This correlation between the amount of intersection line and the extent of breeding of *Anopheles quadrimaculatus* provides for a better understanding and a more intelligent application of water-level management for malaria control.
4. Observations on the relation of water temperatures to the production of anopheline mosquitoes indicate that, in general, when water surface temperatures during the day are above 90° F., *Anopheles quadrimaculatus* predominates and when temperatures are below this, *Anopheles punctipennis* predominates.
5. Observations on the relation of plants to the production of *Anopheles quadrimaculatus* in the reservoirs of the Authority indicate that the littoral plants in this area may be classified into seven general types, each having a different anopheline production potential and presenting different problems with reference to methods of controlling that production. Only one species (*Brasenia schreberi*) of the plants normally occurring in this area appears to be inimical to the production of *Anopheles quadrimaculatus*.
6. Field tests on the distribution of Paris green larvicide by airplane and laboratory tests on relative toxicity and ingestibility indicate that the commercially available Paris greens are, in general, of too fine a particle size for use in airplane dusting. It appears possible to revise particle size specifications and obtain a much more suitable dust without complicating manufacturing procedures.
7. Detailed studies on the life history of *Anopheles quadrimaculatus* have provided useful information with reference to oviposition, mating habits, etc.
8. Observations on the arboricidal treatment of low-stumped black willows indicate that this measure may be successfully used in the dormant winter season or during the growing season.
9. The fiscal year ended June 30, 1943, was the fifth in a program of cooperative malaria research with the University of Tennessee College of Medicine at Memphis. During this year a malaria therapy service was established at the University Hospital which permitted rather significant expansions in research on medical malariology. Considerable emphasis was placed on a project of bioassay of chemotherapeutic agents of possible plasmodicidal value. Other important projects were undertaken in the fields of chemistry, pathology and immunology.

November 6, 1943

MINUTES — 1943

NATIONAL MALARIA SOCIETY

Meeting Conjointly With the Southern Medical Association.

OFFICERS

Honorary President.....Dr. L. O. Howard, Washington, D. C.
President.....Brig. Gen. James S. Simmons, Washington, D. C.
President-elect.....Mr. G. H. Bradley, Atlanta, Georgia
Vice-President.....Mr. J. L. Robertson, Jr., Memphis, Tenn.
Secretary-Treasurer.....Dr. Mark F. Boyd, Tallahassee, Fla.

Tuesday, November 16, 2 p. m.

The National Malaria Society convened in Parlor E of the Gibson Hotel, Cincinnati, Ohio, and was called to order by the President, Brig. Gen. James Simmons. The room soon proving inadequate to accommodate all those desiring to participate in the meeting, the session was adjourned to the foyer of the Ball Room.

The President appointed the following temporary committees, viz: nominations and audit.

The scientific program consisted of seven contributed papers, most of which were illustrated by lantern slides. On the completion of this program there was a brief recess, after which the Society reconvened in business session.

The minutes of the 1942 meeting held in Richmond, Virginia were approved as published in Volume II, No. 1, of the Society's Journal.

The Secretary reported that from the 1942 roster of 207 honorary and active members, one had been lost by death, and 20 dropped for delinquency in dues. There have been 105 active members gained by election, and the names of two delinquents have been restored, giving a current total of 19 honorary and 274 active members on the roster of whom 234 are in good standing as of the date of the report.

The financial report submitted may be summarized as follows:

Balance of Nov. 10, 1942.....	\$ 648.01
Receipts from delinquent, current and advance dues, subscriptions and ad- vertising	1821.30
	<hr/>
	\$2469.31
Expenditures before paying for Vol. II, No. 2, of the Journal.....	843.24
	<hr/>
Balance	\$1626.07

The report also listed assets of \$1,716.57 and liabilities of \$464.00, leaving a balance of \$1,252.57 available for publication purposes in 1944.

Thereupon Mr. Louva Lenert, on behalf of the Auditing Committee, reported that his committee had audited the accounts of the Secretary-Treasurer and found them correct, and introduced a motion, which was adopted, that the report be accepted, and an honorarium of \$75.00 be allowed the Secretary's assistant.

The editor of the Journal, Colonel Charles F. Craig, presented a report on the status of the Journal, and stated that in view of the satisfactory financial position of the Society, quarterly publication of the Journal will be initiated with Vol. III to be issued during 1944, and that the free publication allowance to authors will be slightly increased.

Reports were submitted from the Committees on Medical Research, Epidemiology and Engineering, which were accepted and ordered filed. A proposal from the Committee on Medical Research that the Society standardize malaria terminology was favorably received, and recommendations were requested from the committee.

Dr. Wendell Gingrich, for the Membership Committee, moved that the names of Dr. C. C. Bass and Mr. J. A. LePrince be transferred on the roster from the active to the honorary class, which was adopted.

On behalf of the Nominating Committee, Dr. R. B. Watson submitted the following slate, viz:

Honorary President—Dr. Frederick L. Hoffman, Los Angeles, Calif.

President—Mr. G. H. Bradley, Atlanta, Ga.

President-elect—Mr. H. A. Johnson, Memphis, Tenn.

Vice-President—Mr. Stanley B. Freeborn, Atlanta, Ga.

Secretary-Treasurer—Dr. Mark F. Boyd, Tallahassee, Fla.

Member Editorial Board—Mr. Lloyd Rozeboom, Baltimore, Md.

Representative, Council AAAS—Dr. E. C. Faust, New Orleans, La.

There being no nominations from the floor, a motion was adopted directing the Secretary to cast the unanimous ballot of the Society for the nominees.

The meeting adjourned at 5:20 p. m.

Wednesday, November 17, 2 p. m.

The session was opened by the President in the Victory Room of the Gibson Hotel, and a program of eight contributed papers, mostly illustrated, was presented.

The meeting adjourned at 4:40 p. m.

Thursday, November 18, 2 p. m.

The National Malaria Society convened in joint session with the American Society of Tropical Medicine, in the Florentine Mezzanine of the Gibson Hotel, but immediately adjourned to the Ball Room. Presiding were Brig. Gen. James S. Simmons and Dr. Paul S. Hudson, Presidents of the respective societies.

The program, apart from the President's address entitled "American Mobilization to Combat War-Time Hazards of Malaria," consisted of a series of ten integrated papers presented by invitation, the whole forming a symposium on "A National Program for the Control of Malaria."

At the close of the program a brief recess was held in order to permit the withdrawal of guests, whereupon Mr. Nelson H. Rector, on behalf of the Resolutions Committee, presented the following resolutions:

- (a) In appreciation of the late Dr. Arthur T. McCormack, and
- (b) directing the Secretary to draft letters suitably expressing the Society's thanks for courtesies and hospitality to (1) the Southern Medical Association, (2) the Campbell-Kenton County Medical Society of Kentucky and the Academy of Medicine of Cincinnati, and (3) to the management of the Gibson Hotel, all of which were adopted.

After a further recess, Mr. Rector, on behalf of the Resolutions Committee, presented a further resolution as follows:

WHEREAS: The malaria of the United States is being perpetuated in a limited number of endemic foci and

WHEREAS: It is from these foci that malaria may epidemically extend over large portions of the country and

WHEREAS: The return of soldiers with chronic infections may make future control more difficult and costly.

Therefore, be it resolved that the National Malaria Society endorse the program proposed by Dr. Joseph Mountin of the United States Public Health Service for the final eradication of malaria from the continental United States.

This was adopted and the secretary instructed to furnish a copy to the Surgeon General of the U. S. Public Health Service.

There being no further business, the Society adjourned *sine die*.

